```
=> fil medl
FILE 'MEDLINE' ENTERED AT 15:40:27 ON 25 MAR 2002

  FILE LAST UPDATED: 24 MAR 2002 (20020324/UP). FILE COVERS 1958 TO DATE.

  On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

  MEDLINE now contains IN-PROCESS records. See HELP CONTENT for details.

  MEDLINE is now updated 4 times per week. A new current-awareness alert
  frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

  MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
  MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

  The OLDMEDLINE file segment now contains data from 1958 through 1965.
  Enter HELP CONTENT for details.

  Left, right, and simultaneous left and right truncation are available in the
  Basic Index. See HELP SFIELDS for details.

  THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
  SUBSTANCE IDENTIFICATION.

=> d que l17; d que l56; d que l58; s l17 or l56 or l58
L9       241844 SEA FILE=MEDLINE ABB=ON  ANTI-INFLAMMATORY AGENTS+NT/CT
L10       26167 SEA FILE=MEDLINE ABB=ON  ANGIOGENESIS INHIBITORS+NT/CT
L11       33516 SEA FILE=MEDLINE ABB=ON  DRUG COMBINATIONS/CT
L12       67472 SEA FILE=MEDLINE ABB=ON  DRUG THERAPY, COMBINATION+NT/CT
L13       88096 SEA FILE=MEDLINE ABB=ON  DRUG INTERACTIONS+NT/CT
L14       10574 SEA FILE=MEDLINE ABB=ON  NEOVASCULARIZATION, PATHOLOGIC+NT/CT
L17           1 SEA FILE=MEDLINE ABB=ON  L9 AND L10 AND (L11 OR L12 OR L13)
                AND L14

L10       26167 SEA FILE=MEDLINE ABB=ON  ANGIOGENESIS INHIBITORS+NT/CT
L14       10574 SEA FILE=MEDLINE ABB=ON  NEOVASCULARIZATION, PATHOLOGIC+NT/CT
L15        1455 SEA FILE=MEDLINE ABB=ON  L14(L)(PC OR DT)/CT
L18       92782 SEA FILE=MEDLINE ABB=ON  ANTI-INFLAMMATORY AGENTS, NON-STEROIDA
                L+NT/CT
L20       70126 SEA FILE=MEDLINE ABB=ON  L18(L)(AD OR PK OR PD OR TU)/CT
L49       19334 SEA FILE=MEDLINE ABB=ON  L10(L)(AD OR PD OR PK OR TU)/CT
L52           4 SEA FILE=MEDLINE ABB=ON  L15/MAJ AND L49 AND L20
L53       11764 SEA FILE=MEDLINE ABB=ON  L49/MAJ
L54       32537 SEA FILE=MEDLINE ABB=ON  L20/MAJ
L55           4 SEA FILE=MEDLINE ABB=ON  (L15 AND L53 AND L20) OR (L15 AND L54
                AND L49)
L56           4 SEA FILE=MEDLINE ABB=ON  L52 OR L55

L10       26167 SEA FILE=MEDLINE ABB=ON  ANGIOGENESIS INHIBITORS+NT/CT
L11       33516 SEA FILE=MEDLINE ABB=ON  DRUG COMBINATIONS/CT
L12       67472 SEA FILE=MEDLINE ABB=ON  DRUG THERAPY, COMBINATION+NT/CT
L13       88096 SEA FILE=MEDLINE ABB=ON  DRUG INTERACTIONS+NT/CT
L18       92782 SEA FILE=MEDLINE ABB=ON  ANTI-INFLAMMATORY AGENTS, NON-STEROIDA
                L+NT/CT
L20       70126 SEA FILE=MEDLINE ABB=ON  L18(L)(AD OR PK OR PD OR TU)/CT
L24       51342 SEA FILE=MEDLINE ABB=ON  MACULA?(2A) DEGENERAT? OR RETINOPATH?
                OR GLAUCOMA# OR RETROLENTAL FIBROPLASI? OR VITREORETINOPATH?
L25      125526 SEA FILE=MEDLINE ABB=ON  LEUKEMIA+NT/CT
L26       76307 SEA FILE=MEDLINE ABB=ON  HEMANGIOMA# OR PSORIA? OR KAPOSI? OR
```

Subheadings
DT - drug therapy
PC - prevention & control
AD - administration & dosage
PD - pharmacology
PK - pharmacokinetics
TU - therapeutic use

```
                CROHN? OR ULCERATIVE(A)COLITIS
L27       1357351 SEA FILE=MEDLINE ABB=ON  C4./CT
L28         15823 SEA FILE=MEDLINE ABB=ON  KERATOCONJUNCTIVITIS OR (VITAMIN
                A)(2A)DEFICIEN? OR CONTACT LENS?(3A)OVERWEAR? OR KERATITI?
L29        151447 SEA FILE=MEDLINE ABB=ON  PTERYGI? OR SJOGREN? OR ROSACEA OR
                PHYLECTENULOSIS OR SYPHILI? OR MYCOBACTERI? OR TUBERCULOSIS
L30        194283 SEA FILE=MEDLINE ABB=ON  LIPID#(2A)DEGENERAT? OR (CHEM OR
                CHEMICAL)(2A)BURN# OR ULCER? OR HERPES? OR MARGINAL DEGENERAT?
                OR KERATOLY?
L31         62118 SEA FILE=MEDLINE ABB=ON  ARTHRITIS, RHEUMATOID+NT/CT
L32         27954 SEA FILE=MEDLINE ABB=ON  LUPUS ERYTHEMATOSUS, SYSTEMIC+NT/CT
L33         27202 SEA FILE=MEDLINE ABB=ON  POLYARTERITI? OR SARCOIDO? OR
                SCLERIT? OR STEVENS(A)JOHNSON OR KERATOT? OR PEMPHIGOID#
L34         67982 SEA FILE=MEDLINE ABB=ON  PSEUDOXANTHOMA OR PAGET? OR (VEIN? OR
                ARTER?)(3A)OCCLU? OR UVEITIS OR VITRITIS OR LYME? OR EALE? OR
                BEHCET?
L35          9612 SEA FILE=MEDLINE ABB=ON  HISTOPLASMO?(3A)(EYE# OR OCULAR) OR
                BEST? DISEASE OR MYOPI? OR OPTIC(A)PIT# OR STARGARDT? OR PARS
                (A)PLANITIS
L36         13713 SEA FILE=MEDLINE ABB=ON  RETINA?(2A)DETACH?
L37         16042 SEA FILE=MEDLINE ABB=ON  HYPERVISCOSITY OR TOXOPLASM? OR
                RUBEOSIS
L38           103 SEA FILE=MEDLINE ABB=ON  POST LASER
L49         19334 SEA FILE=MEDLINE ABB=ON  L10(L)(AD OR PD OR PK OR TU)/CT
L50            71 SEA FILE=MEDLINE ABB=ON  L49 AND L20 AND (L24 OR L25 OR L26 OR
                L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33 OR L34 OR L35 OR
                L36 OR L37 OR L38)
L53         11764 SEA FILE=MEDLINE ABB=ON  L49/MAJ
L54         32537 SEA FILE=MEDLINE ABB=ON  L20/MAJ
L58             7 SEA FILE=MEDLINE ABB=ON  (L11 OR L12 OR L13) AND L50 AND (L53
                OR L54)


L141           11 L17 OR L56 OR L58

=> fil hcapl; d que l76; fil embase; d que l85; d que l92; d que l101; s l85 or l92 or
l101
FILE 'HCAPLUS' ENTERED AT 15:41:03 ON 25 MAR 2002
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FILE COVERS 1907 - 25 Mar 2002  VOL 136 ISS 13
FILE LAST UPDATED: 24 Mar 2002  (20020324/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
```

the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

L24	51342	SEA FILE=MEDLINE ABB=ON MACULA?(2A) DEGENERAT? OR RETINOPATH? OR GLAUCOMA# OR RETROLENTAL FIBROPLASI? OR VITREORETINOPATH?
L26	76307	SEA FILE=MEDLINE ABB=ON HEMANGIOMA# OR PSORIA? OR KAPOSI? OR CROHN? OR ULCERATIVE(A)COLITIS
L28	15823	SEA FILE=MEDLINE ABB=ON KERATOCONJUNCTIVITIS OR (VITAMIN A)(2A)DEFICIEN? OR CONTACT LENS?(3A)OVERWEAR? OR KERATITI?
L29	151447	SEA FILE=MEDLINE ABB=ON PTERYGI? OR SJOGREN? OR ROSACEA OR PHYLECTENULOSIS OR SYPHILI? OR MYCOBACTERI? OR TUBERCULOSIS
L30	194283	SEA FILE=MEDLINE ABB=ON LIPID#(2A)DEGENERAT? OR (CHEM OR CHEMICAL)(2A)BURN# OR ULCER? OR HERPES? OR MARGINAL DEGENERAT? OR KERATOLY?
L33	27202	SEA FILE=MEDLINE ABB=ON POLYARTERITI? OR SARCOIDO? OR SCLERIT? OR STEVENS(A)JOHNSON OR KERATOT? OR PEMPHIGOID#
L34	67982	SEA FILE=MEDLINE ABB=ON PSEUDOXANTHOMA OR PAGET? OR (VEIN? OR ARTER?)(3A)OCCLU? OR UVEITIS OR VITRITIS OR LYME? OR EALE? OR BEHCET?
L35	9612	SEA FILE=MEDLINE ABB=ON HISTOPLASMO?(3A)(EYE# OR OCULAR) OR BEST? DISEASE OR MYOPI? OR OPTIC(A)PIT# OR STARGARDT? OR PARS(A)PLANITIS
L36	13713	SEA FILE=MEDLINE ABB=ON RETINA?(2A)DETACH?
L37	16042	SEA FILE=MEDLINE ABB=ON HYPERVISCOSITY OR TOXOPLASM? OR RUBEOSIS
L38	103	SEA FILE=MEDLINE ABB=ON POST LASER
L59	131594	SEA FILE=HCAPLUS ABB=ON L24 OR L26 OR (L28 OR L29 OR L30) OR (L33 OR L34 OR L35 OR L36 OR L37 OR L38)
L60	23157	SEA FILE=HCAPLUS ABB=ON RHEUMATOID(A)ARTHRITIS OR LUPUS(2A)SYSTEMIC OR SICKLE CELL
L61	23964	SEA FILE=HCAPLUS ABB=ON LEUKEMIA+NT/CT
L62	50640	SEA FILE=HCAPLUS ABB=ON TUMOR#/CW
L64	2190	SEA FILE=HCAPLUS ABB=ON ANGIOGENESIS INHIBITORS+RTCS/CT
L65	24493	SEA FILE=HCAPLUS ABB=ON INTERFERON#(A)(ALFA OR ALPHA OR BETA)/OBI OR INTERLEUKIN#(A)12/OBI OR PACLITAXEL OR THALIDOMIDE
L67	22034	SEA FILE=HCAPLUS ABB=ON DRUG INTERACTIONS+OLD,NT/CT
L68	7260	SEA FILE=HCAPLUS ABB=ON (NONSTEROIDAL OR NON STEROIDAL)(L)(ANTIINFLAMMATORY OR ANTI INFLAMMATORY)/OBI OR NSAID#
L69	27105	SEA FILE=HCAPLUS ABB=ON AMINOPYRIN# OR AMODIAQUIN# OR ANTIPYRIN# OR APAZON# OR ASPIRIN OR BENZYDAMIN# OR BUFEXAMAC#
L70	7693	SEA FILE=HCAPLUS ABB=ON CLOFAZIMIN# OR CLONIXIN# OR CURCUMIN# OR DAPSON# OR DICLOFENAC# OR DIFLUNISAL# OR DIPYRON#
L71	35262	SEA FILE=HCAPLUS ABB=ON EPIRIZOL# OR FENOPROFEN# OR FLURBIPROFEN# OR IBUPROFEN# OR INDOMETHACIN# OR KETOROLAC# OR KETOPROFEN#
L72	7413	SEA FILE=HCAPLUS ABB=ON MESALAMIN# OR NAPROXEN# OR OXYPHENBUTAZON# OR PRENAZON# OR PIROXICAM# OR SULFASALAZIN# OR SULINDAC# OR SPROFEN# OR TOLMETIN#
L73	458	SEA FILE=HCAPLUS ABB=ON SUPROFEN#
L74	397	SEA FILE=HCAPLUS ABB=ON (L64 OR L65) AND (L68 OR L69 OR L70 OR L71 OR L72 OR L73)
L75	30	SEA FILE=HCAPLUS ABB=ON L74 AND L67
L76	11	SEA FILE=HCAPLUS ABB=ON (L59 OR L60 OR L61 OR L62) AND L75

— angiogenesis inhibitors, according to Medline

These are all NSAIDs, according to Medline

FILE 'EMBASE' ENTERED AT 15:41:03 ON 25 MAR 2002

FILE COVERS 1974 TO 21 Mar 2002 (20020321/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L79        2424 SEA FILE=EMBASE ABB=ON  ANGIOGENESIS INHIBITOR+NT/CT
L80      164849 SEA FILE=EMBASE ABB=ON  NONSTEROID ANTIINFLAMMATORY AGENT+NT/CT

L85           5 SEA FILE=EMBASE ABB=ON  L79(L)CB/CT AND L80(L)CB/CT
```

subheading CB-drug combination

```
L24       51342 SEA FILE=MEDLINE ABB=ON  MACULA?(2A) DEGENERAT? OR RETINOPATH?
                OR GLAUCOMA# OR RETROLENTAL FIBROPLASI? OR VITREORETINOPATH?
L26       76307 SEA FILE=MEDLINE ABB=ON  HEMANGIOMA# OR PSORIA? OR KAPOSI? OR
                CROHN? OR ULCERATIVE(A)COLITIS
L28       15823 SEA FILE=MEDLINE ABB=ON  KERATOCONJUNCTIVITIS OR (VITAMIN
                A)(2A)DEFICIEN? OR CONTACT LENS?(3A)OVERWEAR? OR KERATITI?
L29      151447 SEA FILE=MEDLINE ABB=ON  PTERYGI? OR SJOGREN? OR ROSACEA OR
                PHYLECTENULOSIS OR SYPHILI? OR MYCOBACTERI? OR TUBERCULOSIS
L30      194283 SEA FILE=MEDLINE ABB=ON  LIPID#(2A)DEGENERAT? OR (CHEM OR
                CHEMICAL)(2A)BURN# OR ULCER? OR HERPES? OR MARGINAL DEGENERAT?
                OR KERATOLY?
L33       27202 SEA FILE=MEDLINE ABB=ON  POLYARTERITI? OR SARCOIDO? OR
                SCLERIT? OR STEVENS(A)JOHNSON OR KERATOT? OR PEMPHIGOID#
L34       67982 SEA FILE=MEDLINE ABB=ON  PSEUDOXANTHOMA OR PAGET? OR (VEIN? OR
                ARTER?)(3A)OCCLU? OR UVEITIS OR VITRITIS OR LYME? OR EALE? OR
                BEHCET?
L35        9612 SEA FILE=MEDLINE ABB=ON  HISTOPLASMO?(3A)(EYE# OR OCULAR) OR
                BEST? DISEASE OR MYOPI? OR OPTIC(A)PIT# OR STARGARDT? OR PARS
                (A)PLANITIS
L36       13713 SEA FILE=MEDLINE ABB=ON  RETINA?(2A)DETACH?
L37       16042 SEA FILE=MEDLINE ABB=ON  HYPERVISCOSITY OR TOXOPLASM? OR
                RUBEOSIS
L38         103 SEA FILE=MEDLINE ABB=ON  POST LASER
L79        2424 SEA FILE=EMBASE ABB=ON  ANGIOGENESIS INHIBITOR+NT/CT
L80      164849 SEA FILE=EMBASE ABB=ON  NONSTEROID ANTIINFLAMMATORY AGENT+NT/CT

L81      104687 SEA FILE=EMBASE ABB=ON  L24 OR L26
L82      220724 SEA FILE=EMBASE ABB=ON  (L28 OR L29 OR L30)
L83      108088 SEA FILE=EMBASE ABB=ON  (L33 OR L34 OR L35 OR L36 OR L37 OR
                L38)
L84       24839 SEA FILE=EMBASE ABB=ON  DRUG POTENTIATION+NT/CT
L86       45062 SEA FILE=EMBASE ABB=ON  RHEUMATOID ARTHRITIS+NT/CT
L87       93935 SEA FILE=EMBASE ABB=ON  LEUKEMIA+NT/CT
L88       20369 SEA FILE=EMBASE ABB=ON  SYSTEMIC LUPUS ERYTHEMATOSUS+NT/CT
L89        8158 SEA FILE=EMBASE ABB=ON  SICKLE CELL ANEMIA+NT/CT
L90          31 SEA FILE=EMBASE ABB=ON  L79 AND L80 AND ((L81 OR L82 OR L83)
                OR (L86 OR L87 OR L88 OR L89))
L91      217495 SEA FILE=EMBASE ABB=ON  DRUG COMBINATION+NT/CT
L92           8 SEA FILE=EMBASE ABB=ON  L90 AND (L91 OR L84)



L80      164849 SEA FILE=EMBASE ABB=ON  NONSTEROID ANTIINFLAMMATORY AGENT+NT/CT
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L96        8167 SEA FILE=EMBASE ABB=ON  "NEOVASCULARIZATION (PATHOLOGY)"+NT/CT

L99         239 SEA FILE=EMBASE ABB=ON  L96(L)(PC OR DT)/CT
L100        181 SEA FILE=EMBASE ABB=ON  L99/MAJ
L101          6 SEA FILE=EMBASE ABB=ON  L100 AND L80/MAJ
```

Subheadings
PC - prevention
DT - drug therapy

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L142         17 L85 OR L92 OR L101

=> fil wpids; d que l125; d que l133; d que l140; s l125 or l133 or l140
FILE 'WPIDS' ENTERED AT 15:41:26 ON 25 MAR 2002
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FILE LAST UPDATED: 21 MAR 2002              <20020321/UP>
MOST RECENT DERWENT UPDATE            200219   <200219/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> SDI'S MAY BE RUN ON EVERY UPDATE OR MONTHLY AS OF JUNE 2001.
    (EVERY UPDATE IS THE DEFAULT). FOR PRICING INFORMATION
    SEE HELP COST <<<

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    RESOURCE, PLEASE VISIT
         http://www.derwent.com/chemistryresource/index.html <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<


L24        51342 SEA FILE=MEDLINE ABB=ON  MACULA?(2A) DEGENERAT? OR RETINOPATH?
                 OR GLAUCOMA# OR RETROLENTAL FIBROPLASI? OR VITREORETINOPATH?
L26        76307 SEA FILE=MEDLINE ABB=ON  HEMANGIOMA# OR PSORIA? OR KAPOSI? OR
                 CROHN? OR ULCERATIVE(A)COLITIS
L28        15823 SEA FILE=MEDLINE ABB=ON  KERATOCONJUNCTIVITIS OR (VITAMIN
                 A)(2A)DEFICIEN? OR CONTACT LENS?(3A)OVERWEAR? OR KERATITI?
L29       151447 SEA FILE=MEDLINE ABB=ON  PTERYGI? OR SJOGREN? OR ROSACEA OR
                 PHYLECTENULOSIS OR SYPHILI? OR MYCOBACTERI? OR TUBERCULOSIS
L30       194283 SEA FILE=MEDLINE ABB=ON  LIPID#(2A)DEGENERAT? OR (CHEM OR
                 CHEMICAL)(2A)BURN# OR ULCER? OR HERPES? OR MARGINAL DEGENERAT?
                 OR KERATOLY?
L33        27202 SEA FILE=MEDLINE ABB=ON  POLYARTERITI? OR SARCOIDO? OR
                 SCLERIT? OR STEVENS(A)JOHNSON OR KERATOT? OR PEMPHIGOID#
L34        67982 SEA FILE=MEDLINE ABB=ON  PSEUDOXANTHOMA OR PAGET? OR (VEIN? OR
                 ARTER?)(3A)OCCLU? OR UVEITIS OR VITRITIS OR LYME? OR EALE? OR
                 BEHCET?
L35         9612 SEA FILE=MEDLINE ABB=ON  HISTOPLASMO?(3A)(EYE# OR OCULAR) OR
                 BEST? DISEASE OR MYOPI? OR OPTIC(A)PIT# OR STARGARDT? OR PARS
                 (A)PLANITIS
L36        13713 SEA FILE=MEDLINE ABB=ON  RETINA?(2A)DETACH?
L37        16042 SEA FILE=MEDLINE ABB=ON  HYPERVISCOSITY OR TOXOPLASM? OR
                 RUBEOSIS
L38          103 SEA FILE=MEDLINE ABB=ON  POST LASER
L69        27105 SEA FILE=HCAPLUS ABB=ON  AMINOPYRIN# OR AMODIAQUIN# OR
                 ANTIPYRIN# OR APAZON# OR ASPIRIN OR BENZYDAMIN# OR BUFEXAMAC#
L70         7693 SEA FILE=HCAPLUS ABB=ON  CLOFAZIMIN# OR CLONIXIN# OR CURCUMIN#
                 OR DAPSON# OR DICLOFENAC# OR DIFLUNISAL# OR DIPYRON#
L71        35262 SEA FILE=HCAPLUS ABB=ON  EPIRIZOL# OR FENOPROFEN# OR FLURBIPROF
                 EN# OR IBUPROFEN# OR INDOMETHACIN# OR KETOROLAC# OR KETOPROFEN#

L72         7413 SEA FILE=HCAPLUS ABB=ON  MESALAMIN# OR NAPROXEN# OR OXYPHENBUTA
                 ZON# OR PRENAZON# OR PIROXICAM# OR SULFASALAZIN# OR SULINDAC#
                 OR SPROFEN# OR TOLMETIN#
```

L73 458 SEA FILE=HCAPLUS ABB=ON SUPROFEN#
L102 16273 SEA FILE=WPIDS ABB=ON L24 OR L26
L103 23771 SEA FILE=WPIDS ABB=ON (L28 OR L29 OR L30)
L104 5608 SEA FILE=WPIDS ABB=ON (L33 OR L34 OR L35 OR L36 OR L37 OR L38)
L105 8387 SEA FILE=WPIDS ABB=ON LEUKEMI? OR LEUKAEMI?
L106 3262 SEA FILE=WPIDS ABB=ON SICKLE CELL OR SYSTEMIC(2A)LUPUS
L107 9146 SEA FILE=WPIDS ABB=ON RHEUMATOID ARTHRITI?
L109 5278 SEA FILE=WPIDS ABB=ON (L69 OR L70 OR L71 OR L72 OR L73)
L110 465 SEA FILE=WPIDS ABB=ON (NEOVASCULARI? OR ANGIOGENESIS)(2A)(INHIBITOR# OR ANTAGONIST#)
L114 55899 SEA FILE=WPIDS ABB=ON NEOPLAS? OR TUMOR# OR TUMOUR# OR CANCER?
L116 420234 SEA FILE=WPIDS ABB=ON COMBIN? OR SYNERG?
L121 1909 SEA FILE=WPIDS ABB=ON INTERFERON#(A)(ALFA OR ALPHA OR BETA) OR (IL OR INTERLEUKIN#)(A)12 OR IL12 OR PACLITAXEL OR THALIDOMID#
L123 1720 SEA FILE=WPIDS ABB=ON (NONSTEROIDAL OR NON STEROIDAL)(2A)(ANTI INFLAMMATORY OR ANTI INFLAMMATORY) OR NSAID#
L124 66 SEA FILE=WPIDS ABB=ON (L123 OR L109)(S)(L110 OR L121)
L125 7 SEA FILE=WPIDS ABB=ON L124(S)L116(S)((L102 OR L103 OR L104 OR L105 OR L106 OR L107) OR L114)

L24 51342 SEA FILE=MEDLINE ABB=ON MACULA?(2A) DEGENERAT? OR RETINOPATH? OR GLAUCOMA# OR RETROLENTAL FIBROPLASI? OR VITREORETINOPATH?
L26 76307 SEA FILE=MEDLINE ABB=ON HEMANGIOMA# OR PSORIA? OR KAPOSI? OR CROHN? OR ULCERATIVE(A)COLITIS
L28 15823 SEA FILE=MEDLINE ABB=ON KERATOCONJUNCTIVITIS OR (VITAMIN A)(2A)DEFICIEN? OR CONTACT LENS?(3A)OVERWEAR? OR KERATITI?
L29 151447 SEA FILE=MEDLINE ABB=ON PTERYGI? OR SJOGREN? OR ROSACEA OR PHYLECTENULOSIS OR SYPHILI? OR MYCOBACTERI? OR TUBERCULOSIS
L30 194283 SEA FILE=MEDLINE ABB=ON LIPID#(2A)DEGENERAT? OR (CHEM OR CHEMICAL)(2A)BURN# OR ULCER? OR HERPES? OR MARGINAL DEGENERAT? OR KERATOLY?
L33 27202 SEA FILE=MEDLINE ABB=ON POLYARTERITI? OR SARCOIDO? OR SCLERIT? OR STEVENS(A)JOHNSON OR KERATOT? OR PEMPHIGOID#
L34 67982 SEA FILE=MEDLINE ABB=ON PSEUDOXANTHOMA OR PAGET? OR (VEIN? OR ARTER?)(3A)OCCLU? OR UVEITIS OR VITRITIS OR LYME? OR EALE? OR BEHCET?
L35 9612 SEA FILE=MEDLINE ABB=ON HISTOPLASMO?(3A)(EYE# OR OCULAR) OR BEST? DISEASE OR MYOPI? OR OPTIC(A)PIT# OR STARGARDT? OR PARS(A)PLANITIS
L36 13713 SEA FILE=MEDLINE ABB=ON RETINA?(2A)DETACH?
L37 16042 SEA FILE=MEDLINE ABB=ON HYPERVISCOSITY OR TOXOPLASM? OR RUBEOSIS
L38 103 SEA FILE=MEDLINE ABB=ON POST LASER
L69 27105 SEA FILE=HCAPLUS ABB=ON AMINOPYRIN# OR AMODIAQUIN# OR ANTIPYRIN# OR APAZON# OR ASPIRIN OR BENZYDAMIN# OR BUFEXAMAC#
L70 7693 SEA FILE=HCAPLUS ABB=ON CLOFAZIMIN# OR CLONIXIN# OR CURCUMIN# OR DAPSON# OR DICLOFENAC# OR DIFLUNISAL# OR DIPYRON#
L71 35262 SEA FILE=HCAPLUS ABB=ON EPIRIZOL# OR FENOPROFEN# OR FLURBIPROFEN# OR IBUPROFEN# OR INDOMETHACIN# OR KETOROLAC# OR KETOPROFEN#
L72 7413 SEA FILE=HCAPLUS ABB=ON MESALAMIN# OR NAPROXEN# OR OXYPHENBUTAZON# OR PRENAZON# OR PIROXICAM# OR SULFASALAZIN# OR SULINDAC# OR SPROFEN# OR TOLMETIN#
L73 458 SEA FILE=HCAPLUS ABB=ON SUPROFEN#
L102 16273 SEA FILE=WPIDS ABB=ON L24 OR L26
L103 23771 SEA FILE=WPIDS ABB=ON (L28 OR L29 OR L30)
L104 5608 SEA FILE=WPIDS ABB=ON (L33 OR L34 OR L35 OR L36 OR L37 OR L38)

L105 8387 SEA FILE=WPIDS ABB=ON LEUKEMI? OR LEUKAEMI?
L106 3262 SEA FILE=WPIDS ABB=ON SICKLE CELL OR SYSTEMIC(2A)LUPUS
L107 9146 SEA FILE=WPIDS ABB=ON RHEUMATOID ARTHRITI?
L109 5278 SEA FILE=WPIDS ABB=ON (L69 OR L70 OR L71 OR L72 OR L73)
L123 1720 SEA FILE=WPIDS ABB=ON (NONSTEROIDAL OR NON STEROIDAL)(2A)(ANTI INFLAMMATORY OR ANTI INFLAMMATORY) OR NSAID#
L126 3029 SEA FILE=WPIDS ABB=ON ANGIOGENESIS OR NEOVASCULARI?
L128 854 SEA FILE=WPIDS ABB=ON L126(5A)(PREVENT? OR INHIBIT OR INHIBITION)
L132 497 SEA FILE=WPIDS ABB=ON (L123 OR L109)(L)(TREAT? OR THERAP?)/TI

L133 3 SEA FILE=WPIDS ABB=ON L132 AND L128 AND (L102 OR L103 OR L104 OR L105 OR L106 OR L107)

L24 51342 SEA FILE=MEDLINE ABB=ON MACULA?(2A) DEGENERAT? OR RETINOPATH? OR GLAUCOMA# OR RETROLENTAL FIBROPLASI? OR VITREORETINOPATH?
L26 76307 SEA FILE=MEDLINE ABB=ON HEMANGIOMA# OR PSORIA? OR KAPOSI? OR CROHN? OR ULCERATIVE(A)COLITIS
L28 15823 SEA FILE=MEDLINE ABB=ON KERATOCONJUNCTIVITIS OR (VITAMIN A)(2A)DEFICIEN? OR CONTACT LENS?(3A)OVERWEAR? OR KERATITI?
L29 151447 SEA FILE=MEDLINE ABB=ON PTERYGI? OR SJOGREN? OR ROSACEA OR PHYLECTENULOSIS OR SYPHILI? OR MYCOBACTERI? OR TUBERCULOSIS
L30 194283 SEA FILE=MEDLINE ABB=ON LIPID#(2A)DEGENERAT? OR (CHEM OR CHEMICAL)(2A)BURN# OR ULCER? OR HERPES? OR MARGINAL DEGENERAT? OR KERATOLY?
L33 27202 SEA FILE=MEDLINE ABB=ON POLYARTERITI? OR SARCOIDO? OR SCLERIT? OR STEVENS(A)JOHNSON OR KERATOT? OR PEMPHIGOID#
L34 67982 SEA FILE=MEDLINE ABB=ON PSEUDOXANTHOMA OR PAGET? OR (VEIN? OR ARTER?)(3A)OCCLU? OR UVEITIS OR VITRITIS OR LYME? OR EALE? OR BEHCET?
L35 9612 SEA FILE=MEDLINE ABB=ON HISTOPLASMO?(3A)(EYE# OR OCULAR) OR BEST? DISEASE OR MYOPI? OR OPTIC(A)PIT# OR STARGARDT? OR PARS(A)PLANITIS
L36 13713 SEA FILE=MEDLINE ABB=ON RETINA?(2A)DETACH?
L37 16042 SEA FILE=MEDLINE ABB=ON HYPERVISCOSITY OR TOXOPLASM? OR RUBEOSIS
L38 103 SEA FILE=MEDLINE ABB=ON POST LASER
L69 27105 SEA FILE=HCAPLUS ABB=ON AMINOPYRIN# OR AMODIAQUIN# OR ANTIPYRIN# OR APAZON# OR ASPIRIN OR BENZYDAMIN# OR BUFEXAMAC#
L70 7693 SEA FILE=HCAPLUS ABB=ON CLOFAZIMIN# OR CLONIXIN# OR CURCUMIN# OR DAPSON# OR DICLOFENAC# OR DIFLUNISAL# OR DIPYRON#
L71 35262 SEA FILE=HCAPLUS ABB=ON EPIRIZOL# OR FENOPROFEN# OR FLURBIPROFEN# OR IBUPROFEN# OR INDOMETHACIN# OR KETOROLAC# OR KETOPROFEN#
L72 7413 SEA FILE=HCAPLUS ABB=ON MESALAMIN# OR NAPROXEN# OR OXYPHENBUTAZON# OR PRENAZON# OR PIROXICAM# OR SULFASALAZIN# OR SULINDAC# OR SPROFEN# OR TOLMETIN#
L73 458 SEA FILE=HCAPLUS ABB=ON SUPROFEN#
L102 16273 SEA FILE=WPIDS ABB=ON L24 OR L26
L103 23771 SEA FILE=WPIDS ABB=ON (L28 OR L29 OR L30)
L104 5608 SEA FILE=WPIDS ABB=ON (L33 OR L34 OR L35 OR L36 OR L37 OR L38)
L105 8387 SEA FILE=WPIDS ABB=ON LEUKEMI? OR LEUKAEMI?
L106 3262 SEA FILE=WPIDS ABB=ON SICKLE CELL OR SYSTEMIC(2A)LUPUS
L107 9146 SEA FILE=WPIDS ABB=ON RHEUMATOID ARTHRITI?
L109 5278 SEA FILE=WPIDS ABB=ON (L69 OR L70 OR L71 OR L72 OR L73)
L123 1720 SEA FILE=WPIDS ABB=ON (NONSTEROIDAL OR NON STEROIDAL)(2A)(ANTI INFLAMMATORY OR ANTI INFLAMMATORY) OR NSAID#
L126 3029 SEA FILE=WPIDS ABB=ON ANGIOGENESIS OR NEOVASCULARI?
L128 854 SEA FILE=WPIDS ABB=ON L126(5A)(PREVENT? OR INHIBIT OR INHIBITION)

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L134        3221 SEA FILE=WPIDS ABB=ON  (L123 OR L109) AND B05/DC
L135        3455 SEA FILE=WPIDS ABB=ON  A61K031/IC AND (L123 OR L109)
L136        2063 SEA FILE=WPIDS ABB=ON  L134 AND L135
L140           2 SEA FILE=WPIDS ABB=ON  L128 AND (L102 OR L103 OR L104 OR L105
               OR L106 OR L107) AND L136 AND CANCER/TI


L143          10 L125 OR L133 OR L140

=> dup rem l141,l76,l142,l143
FILE 'MEDLINE' ENTERED AT 15:42:03 ON 25 MAR 2002

FILE 'HCAPLUS' ENTERED AT 15:42:03 ON 25 MAR 2002
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PROCESSING COMPLETED FOR L141
PROCESSING COMPLETED FOR L76
PROCESSING COMPLETED FOR L142
PROCESSING COMPLETED FOR L143
L144          43 DUP REM L141 L76 L142 L143 (6 DUPLICATES REMOVED)
                 ANSWERS '1-11' FROM FILE MEDLINE
                 ANSWERS '12-22' FROM FILE HCAPLUS
                 ANSWERS '23-37' FROM FILE EMBASE
                 ANSWERS '38-43' FROM FILE WPIDS

=> d ibib ab 1-43; fil hom

L144 ANSWER 1 OF 43     MEDLINE                          DUPLICATE 4
ACCESSION NUMBER:   2000011629     MEDLINE
DOCUMENT NUMBER:    20011629   PubMed ID: 10544394
TITLE:              Topical amiloride accelerates healing and delays
                    neovascularization in mechanically produced corneal ulcers
                    in rabbits.
AUTHOR:             Sood A K; Gupta B; Chugh P
CORPORATE SOURCE:   Department of Ophthalmology, LLRM Medical College, Meerut,
                    India.
SOURCE:             METHODS AND FINDINGS IN EXPERIMENTAL AND CLINICAL
                    PHARMACOLOGY, (1999 Sep) 21 (7) 491-7.
                    Journal code: LZN; 7909595. ISSN: 0379-0355.
PUB. COUNTRY:       Spain
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199912
ENTRY DATE:         Entered STN: 20000113
                    Last Updated on STN: 20000113
                    Entered Medline: 19991203
AB  The present investigation was undertaken to explore the ulcer healing and
    antiangiogenic efficacy of two dosage schedules of topically administered
    amiloride in mechanically produced corneal ulcers in rabbits and to
    compare its effect with the conventional topical antiinflammatory
    angiostatic agent flurbiprofen. The epithelium and superficial lamellae of
    the stroma of both eyes of each rabbit were cut through by a corneal
    trephine (8 mm diameter) up to a depth of 0.3 mm and removed after local
    anesthesia. The animals were randomly divided in groups of 4 rabbits each.
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In the eyes of 2 groups of animals, amiloride (4%) was instilled either q.i.d. or b.i.d.; in another, flurbiprofen (0.03%) was instilled twice daily whereas the saline-treated group served as control. The healing of ulcer was followed on a slit lamp regarding its size, depth, slough formation, infiltration and neovascularization on alternate days up to the 10th day with and without fluorescein staining. Healing of corneal ulcers was significantly accelerated by both dosage schedules of topical amiloride (4%) but more so following q.i.d. instillation. Topical flurbiprofen, on the other hand, delayed the healing process. Instillation of amiloride four times daily or flurbiprofen twice daily inhibited angiogenesis significantly. However, appearance of new vessels was completely prevented when amiloride (4%) was instilled twice daily. Thus topical amiloride (4%) may prove to be a cheap and better antineovascularization as well as ulcer healing agent with no apparent side effects. Inhibition of uPA by amiloride appears to be responsible for these effects.

L144 ANSWER 2 OF 43 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999335187 MEDLINE
DOCUMENT NUMBER: 99335187 PubMed ID: 10408702
TITLE: Combination oral antiangiogenic therapy with thalidomide and sulindac inhibits tumour growth in rabbits.
AUTHOR: Verheul H M; Panigrahy D; Yuan J; D'Amato R J
CORPORATE SOURCE: Department of Surgery, Children's Hospital, Harvard Medical School, Boston, MA 02115, USA.
SOURCE: BRITISH JOURNAL OF CANCER, (1999 Jan) 79 (1) 114-8. Journal code: AV4; 0370635. ISSN: 0007-0920.
PUB. COUNTRY: SCOTLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990806
Last Updated on STN: 19990806
Entered Medline: 19990729

AB Neovascularization facilitates tumour growth and metastasis formation. In our laboratory, we attempt to identify clinically available oral efficacious drugs for antiangiogenic activity. Here, we report which non-steroidal anti-inflammatory drugs (NSAIDs) can inhibit corneal neovascularization, induced by basic fibroblast growth factor (bFGF) or vascular endothelial growth factor (VEGF). This antiangiogenic activity may contribute to the known effects of NSAIDs on gastric ulcers, polyps and tumours. We found that sulindac was one of the most potent antiangiogenic NSAIDs, inhibiting bFGF-induced neovascularization by 50% and VEGF-induced neovascularization by 55%. Previously, we reported that thalidomide inhibited growth factor-induced corneal neovascularization. When we combined sulindac with thalidomide, we found a significantly increased inhibition of bFGF- or VEGF-induced corneal neovascularization (by 63% or 74% respectively) compared with either agent alone ($P < 0.01$). Because of this strong antiangiogenic effect, we tested the oral combination of thalidomide and sulindac for its ability to inhibit the growth of V2 carcinoma in rabbits. Oral treatment of thalidomide or sulindac alone inhibited tumour growth by 55% and 35% respectively. When given together, the growth of the V2 carcinoma was inhibited by 75%. Our results indicated that oral antiangiogenic combination therapy with thalidomide and sulindac may be a useful non-toxic treatment for cancer.

L144 ANSWER 3 OF 43 MEDLINE
ACCESSION NUMBER: 2002063627 MEDLINE
DOCUMENT NUMBER: 21634508 PubMed ID: 11772931
TITLE: Angioprevention': angiogenesis is a common and key target for cancer chemopreventive agents.
AUTHOR: Tosetti Francesca; Ferrari Nicolette; De Flora Silvio;

Albini Adriana
CORPORATE SOURCE: Molecular Biology Laboratory, National Cancer Research Institute (IST), Genova, Italy.
SOURCE: FASEB JOURNAL, (2002 Jan) 16 (1) 2-14. Ref: 158
Journal code: 8804484. ISSN: 1530-6860.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020201
Entered Medline: 20020131

AB The potential to block tumor growth by inhibition of the neoangiogenic process represents an intriguing approach to the treatment of solid tumors. The high proliferation rate in the tumor deprived of proper vascularization would be balanced by cell death due to lack of diffusion of nutrients and oxygen. Matrix metalloproteinases (MMPs), angiogenic growth factors, and their receptors are the main targets of an increasing number of clinical trials approved to test the tolerance and therapeutic efficacy of antiangiogenic agents. We observed that a series of substances proposed as possible cancer chemopreventive agents show antiangiogenic properties when tested in in vitro and in vivo angiogenesis models. We demonstrated that N-acetyl-l-cysteine is able to reduce the invasive and metastatic potential of melanoma cells, and to inhibit endothelial cell invasion by direct inhibition of MMP activity. We also showed that epigallocatechin gallate (EGCG), a flavonoid from green tea that possesses chemopreventive activity in experimental and epidemiological studies, is a potent inhibitor of MMP-2 and MMP-9. Angiogenesis has also been demonstrated to be a target for nonsteroidal anti-inflammatory drug chemopreventive activity. Based on these data, we hypothesize that other chemopreventive agents, including natural or synthetic retinoids, steroid hormone antagonists, peroxisome proliferator-activated receptor gamma ligands, vitamin D, and protease inhibitors, might have antiangiogenesis as an important mechanism of action, a novel concept we will term 'angioprevention'. We analyze the mechanisms on how and why chemopreventive agents could exert antiangiogenic effects aimed at controlling tumor growth, and their potential use in the clinic.

L144 ANSWER 4 OF 43 MEDLINE
ACCESSION NUMBER: 2000209416 MEDLINE
DOCUMENT NUMBER: 20209416 PubMed ID: 10744729
TITLE: Curcuminoids inhibit the angiogenic response stimulated by fibroblast growth factor-2, including expression of matrix metalloproteinase gelatinase B.
AUTHOR: Mohan R; Sivak J; Ashton P; Russo L A; Pham B Q; Kasahara N; Raizman M B; Fini M E
CORPORATE SOURCE: Vision Research Laboratories of New England Eye Center and the Department of Ophthalmology, Tufts University School of Medicine, Boston, Massachusetts 02111, USA.
CONTRACT NUMBER: AR42981 (NIAMS)
EY12651 (NEI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Apr 7) 275 (14) 10405-12.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518

Last Updated on STN: 20000518
Entered Medline: 20000508

AB We have studied mechanisms controlling activation of the gelatinase B gene (matrix metalloproteinase-9) by fibroblast growth factor-2 (FGF-2) during angiogenesis, and the effects of the natural product curcuminoids on this process. Using a transgenic mouse (line 3445) harboring a gelatinase B promoter/lacZ fusion gene, we demonstrate FGF-2 stimulation of reporter gene expression in endothelial cells of invading neocapillaries in the corneal micropocket assay. Using cultured corneal cells, we show that FGF-2 stimulates DNA binding activity of transcription factor AP-1 but not NF-kappaB and that AP-1 stimulation is inhibited by curcuminoids. We further show that induction of gelatinase B transcriptional promoter activity in response to FGF-2 is dependent on AP-1 but not NF-kappaB response elements and that promoter activity is also inhibited by curcuminoids. In rabbit corneas, the angiogenic response induced by implantation of an FGF-2 pellet is inhibited by the co-implantation of a curcuminoid pellet, and this correlates with inhibition of endogenous gelatinase B expression induced by FGF-2. Angiostatic efficacy in the cornea is also observed when curcuminoids are provided to mice in the diet. Our findings provide evidence that curcuminoids target the FGF-2 angiogenic signaling pathway and inhibit expression of gelatinase B in the angiogenic process.

L144 ANSWER 5 OF 43 MEDLINE
ACCESSION NUMBER: 2000474166 MEDLINE
DOCUMENT NUMBER: 20420242 PubMed ID: 10962577
TITLE: Paclitaxel sensitivity of breast cancer cells with constitutively active NF-kappaB is enhanced by IkappaBalpha super-repressor and parthenolide.
AUTHOR: Patel N M; Nozaki S; Shortle N H; Bhat-Nakshatri P; Newton T R; Rice S; Gelfanov V; Boswell S H; Goulet R J Jr; Sledge G W Jr; Nakshatri H
CORPORATE SOURCE: Department of Surgery, Indiana University School of Medicine, Indianapolis, Indiana, IN 46202, USA.
SOURCE: ONCOGENE, (2000 Aug 24) 19 (36) 4159-69.
Journal code: ONC; 8711562. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001012
Last Updated on STN: 20001012
Entered Medline: 20001002

AB The transcription factor nuclear factor-kappaB (NF-kappaB) regulates genes important for tumor invasion, metastasis and chemoresistance. Normally, NF-kappaB remains sequestered in an inactive state by cytoplasmic inhibitor-of-kappaB (IkappaB) proteins. NF-kappaB translocates to nucleus and activates gene expression upon exposure of cells to growth factors and cytokines. We and others have shown previously that NF-kappaB is constitutively active in a subset of breast cancers. In this study, we show that constitutive activation of NF-kappaB leads to overexpression of the anti-apoptotic genes c-inhibitor of apoptosis 2 (c-IAP2) and manganese superoxide dismutase (Mn-SOD) in breast cancer cells. Furthermore, expression of the anti-apoptotic tumor necrosis factor receptor associated factor 1 (TRAF1) and defender-against cell death (DAD-1) is regulated by NF-kappaB in certain breast cancer cells. We also demonstrate that NF-kappaB-inducible genes protect cancer cells against paclitaxel as MDA-MB-231 breast cancer cells modified to overexpress IkappaBalpha required lower concentrations of paclitaxel to arrest at the G2/M phase of the cell cycle and undergo apoptosis when compared to parental cells. The effect of NF-kappaB on paclitaxel-sensitivity appears to be specific to cancer cells because normal fibroblasts derived from embryos lacking p65

subunit of NF-kappaB and wild type littermate embryos were insensitive to paclitaxel-induced G2/M cell cycle arrest. Parthenolide, an active ingredient of herbal remedies such as feverfew (tanacetum parthenium), mimicked the effects of IkappaBalpha by inhibiting NF-kappaB DNA binding activity and Mn-SOD expression, and increasing paclitaxel-induced apoptosis of breast cancer cells. These results suggest that active ingredients of herbs with anti-inflammatory properties may be useful in increasing the sensitivity of cancers with constitutively active NF-kappaB to chemotherapeutic drugs. Oncogene (2000) 19, 4159 - 4169

L144 ANSWER 6 OF 43 MEDLINE
ACCESSION NUMBER: 2000199678 MEDLINE
DOCUMENT NUMBER: 20199678 PubMed ID: 10737417
TITLE: Interleukin 12 and indomethacin exert a synergistic, angiogenesis-dependent antitumor activity in mice.
AUTHOR: Golab J; Kozar K; Kaminski R; Czajka A; Marczak M; Switaj T; Giermasz A; Stoklosa T; Lasek W; Zagozdzon R; Mucha K; Jakobisiak M
CORPORATE SOURCE: Department of Immunology, Institute of Biostructure, The Medical University of Warsaw, Poland.. jgolab@ib.amwaw.edu.pl
SOURCE: LIFE SCIENCES, (2000 Feb 18) 66 (13) 1223-30. Journal code: L62; 0375521. ISSN: 0024-3205.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000421
Last Updated on STN: 20000518
Entered Medline: 20000411

AB Nonsteroidal anti-inflammatory drugs have been shown to reduce the incidence and mortality from colorectal cancer. It has recently been demonstrated that these drugs are capable of suppressing the production of pro-angiogenic factors from tumor cells. The mechanisms of antitumor action of interleukin 12 include the enforced secretion of anti-angiogenic factors and stimulation of antitumor immunity. Therefore, we hypothesized that the combination of a model nonsteroidal anti-inflammatory drug--indomethacin and interleukin 12--would result in enhanced angiogenesis-dependent antitumor effects against a colon-26 carcinoma cells transplanted into syngeneic mice. As expected the combined administration of both agents simultaneously resulted in a strengthened antitumor activity that was manifested as a retardation of tumor growth and prolongation of mouse survival. Importantly some mice were completely cured after the combined treatment. As administration of interleukin 12 and indomethacin resulted in enhanced inhibition of angiogenesis it seems possible that prevention of new blood vessel formation is one of the mechanisms responsible for the observed antitumor effects.

L144 ANSWER 7 OF 43 MEDLINE
ACCESSION NUMBER: 97015611 MEDLINE
DOCUMENT NUMBER: 97015611 PubMed ID: 8862260
TITLE: Effect of rhuIFN-gamma treatment in multibacillary leprosy patients.
AUTHOR: Sampaio E P; Malta A M; Sarno E N; Kaplan G
CORPORATE SOURCE: Leprosy Laboratory, Oswaldo Cruz Institute, Fiocruz, Manguinhos, Rio de Janeiro, Brazil.
CONTRACT NUMBER: AI-33124 (NIAID)
SOURCE: INTERNATIONAL JOURNAL OF LEPROSY AND OTHER MYCOBACTERIAL DISEASES, (1996 Sep) 64 (3) 268-73. Journal code: INU; 8505819. ISSN: 0148-916X.
PUB. COUNTRY: United States
(CLINICAL TRIAL)

(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961209

AB Previous studies have shown that when multibacillary leprosy patients were treated with recombinant human interferon gamma (rhuIFN-gamma) for 6-10 months there was an accelerated reduction in the number of acid-fast bacilli in the skin at the site of injection as well as an accelerated bacillary reduction at distal sites. However, this favorable out-come of IFN-gamma treatment was associated with the development of erythema nodosum leprosum (ENL). The present study was undertaken to investigate whether rhuIFN-gamma-induced bacillary clearance could be disassociated from the induction of ENL. rhuIFN-gamma was administered together with thalidomide and conventional multidrug chemotherapy to newly diagnosed leprosy patients. During treatment with this combination of drugs, the mean reduction in bacterial load was the same as the reduction observed with chemotherapy alone. Moreover, the inclusion of thalidomide in the treatment regimen was associated with a low frequency of ENL episodes. A second group of leprosy patients, who had already completed 2 years of chemotherapy, were treated with rhuIFN-gamma only. In those patients who were skin bacilli negative, ENL did not occur during rhuIFN-gamma treatment. In contrast, in bacilli-positive patients the frequency of ENL during rhuIFN-gamma treatment was higher, as was the occurrence of local erythema and induration. However, rhuIFN-gamma treatment without concomitant chemotherapy did not result in a reduction in the bacterial load in the skin of bacilli-positive patients. These findings, taken together, indicate that rhuIFN-gamma does not, by itself, accelerate bacterial clearance, but requires concomitant chemotherapy to achieve the accelerated reduction in bacillary load. Thalidomide reduces the frequency of IFN-gamma-induced ENL, but also eliminates the IFN-gamma-induced bacillary clearance.

L144 ANSWER 8 OF 43 MEDLINE
ACCESSION NUMBER: 2001280523 MEDLINE
DOCUMENT NUMBER: 97702048 PubMed ID: 11363915
TITLE: Pot shots.
AUTHOR: Anonymous
SOURCE: NOTES FROM THE UNDERGROUND, (1996 Sep) (No 33) 6.
Journal code: 9300979.
PUB. COUNTRY: United States
(NEWSPAPER ARTICLE)
LANGUAGE: English
FILE SEGMENT: AIDS
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20020222
Entered Medline: 19961212

AB Certain HIV drugs have significant side effects. There have been reports from Europe that some hemophiliacs using protease inhibitors suffered from spontaneous bleeding. Clofazimine, sold as Lamprene, has been shown to cause harm when used with clarithromycin and ethambutol to treat MAC. Lamprene may cause internal bleeding, nausea, diarrhea, dizziness, drowsiness, and dry skin. Results of a Taiwanese trial of thymosin-alpha indicate that it did not help treat Hepatitis B in a statistically significant way. NAC, an antioxidant, may increase glutathione levels and indirectly increase survival.

L144 ANSWER 9 OF 43 MEDLINE
ACCESSION NUMBER: 93088226 MEDLINE

DOCUMENT NUMBER: 93088226 PubMed ID: 1280861
TITLE: [The use of interferon in the combined therapy of juvenile rheumatoid arthritis].
Ispol'zovanie interferona v kompleksnoi terapii iuvenil'nogo revmatoidnogo artrita.
AUTHOR: Shcherbakova M Iu; Kuz'mina N N; Malinovskaia V V; Gevorkian M G
SOURCE: TERAPEVTICHESKII ARKHIV, (1992) 64 (5) 36-40.
Journal code: VLU; 2984818R. ISSN: 0040-3660.
PUB. COUNTRY: RUSSIA: Russian Federation
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199301
ENTRY DATE: Entered STN: 19930129
Last Updated on STN: 20000303
Entered Medline: 19930106

AB The efficacy of recombinant gene engineering alpha 2-interferon (reaferon) was studied and compared in 60 patients suffering from verified juvenile rheumatoid arthritis (JRA). Reaferon was shown to possess good tolerance and to produce an adequate therapeutic effect. The combined use of reaferon and methotrexate permits potentiating the therapeutic effect of interferon and avoiding side effects seen with methotrexate used alone. Besides, it makes it possible to reduce the incidence of respiratory infections which are often associated with exacerbation of the underlying disease when treated by conventional methods.

L144 ANSWER 10 OF 43 MEDLINE
ACCESSION NUMBER: 90371488 MEDLINE
DOCUMENT NUMBER: 90371488 PubMed ID: 2396216
TITLE: [The comparative efficacy of reaferon and methotrexate in rheumatoid arthritis].
Sravnitel'naia effektivnost' reaferona i metotreksata pri revmatoidnom artrite.
AUTHOR: Seilanov L S; Balabanova R M; Denisov L A
SOURCE: TERAPEVTICHESKII ARKHIV, (1990) 62 (5) 41-4.
Journal code: VLU; 2984818R. ISSN: 0040-3660.
PUB. COUNTRY: USSR
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199010
ENTRY DATE: Entered STN: 19901109
Last Updated on STN: 20000303
Entered Medline: 19901011

L144 ANSWER 11 OF 43 MEDLINE
ACCESSION NUMBER: 75114452 MEDLINE
DOCUMENT NUMBER: 75114452 PubMed ID: 1090562
TITLE: [Therapeutic experience on the effect of thalidomidomide on lepra reaction].
Therapeutische Erfahrungen uber den Einfluss des Thalidomids bei der Lepra-Reaktion.
AUTHOR: Sheskin J
SOURCE: HAUTARZT, (1975 Jan) 26 (1) 1-5.
Journal code: G13; 0372755. ISSN: 0017-8470.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197506
ENTRY DATE: Entered STN: 19900310

Last Updated on STN: 19900310
Entered Medline: 19750613

L144 ANSWER 12 OF 43 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2001:247189 HCAPLUS
DOCUMENT NUMBER: 134:247240
TITLE: Prevention of colorectal cancer with a cyclooxygenase inhibitor, a vitamin D3 or analog, and calcium.
INVENTOR(S): Raskov, Hans Henrik
PATENT ASSIGNEE(S): Colotech A/S, Den.
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001022974	A1	20010405	WO 2000-DK546	20000929
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001049364	A1	20011206	US 2001-825891	20010405

PRIORITY APPLN. INFO.: DK 1999-1390 A 19990929
WO 2000-DK546 A1 20000929

AB A method for prevention of colorectal cancer or the initiation and/or progression of colorectal cancer in a human comprises administration of a combination dosage of a cyclooxygenase (COX) inhibitor, a vitamin D3, including analogs and metabolites thereof, and calcium. In a further embodiment, the invention relates to the use of the combination dosage for the prepn. of a medicament and to such pharmaceutical prepns. In a further aspect, the invention provides a method for reducing the effective dosage of **aspirin** in a chemoprophylactive treatment of colorectal cancer in a human by co-administration with a nontoxic dosage of a vitamin D3, including analogs and metabolites thereof, and calcium in the form of a combination dosage.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L144 ANSWER 13 OF 43 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 2000:456916 HCAPLUS
DOCUMENT NUMBER: 133:68929
TITLE: Use of a matrix metalloproteinase inhibitor and an integrin antagonist in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G. D. Searle & Co., USA
SOURCE: PCT Int. Appl., 358 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038719	A1	20000706	WO 1999-US30700	19991222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1140183	A1	20011010	EP 1999-968942	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
WO 1999-US30700 W 19991222

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a matrix metalloproteinase inhibitor, an integrin antagonist, and an antineoplastic agent.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L144 ANSWER 14 OF 43 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 2000:456915 HCAPLUS
DOCUMENT NUMBER: 133:84242
TITLE: Method of using a matrix metalloproteinase inhibitor and one or more antineoplastic agents as a combination therapy in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle & Co., USA
SOURCE: PCT Int. Appl., 277 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038718	A2	20000706	WO 1999-US30699	19991222
WO 2000038718	A3	20001109		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1140182	A2	20011010	EP 1999-968941	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
WO 1999-US30699 W 19991222

AB Methods are provided for the prevention and treatment of neoplasia disorders in a mammal using a combination of a matrix metalloproteinase inhibitor and an antineoplastic agent.

L144 ANSWER 15 OF 43 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 6

ACCESSION NUMBER: 1998:341491 HCAPLUS
DOCUMENT NUMBER: 129:12742
TITLE: Methods and compositions using **thalidomide** or other angiogenesis-inhibitory compound and anti-inflammatory agent for inhibition of angiogenesis
INVENTOR(S): D'Amato, Robert J.
PATENT ASSIGNEE(S): Children's Medical Center, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9819649	A2	19980514	WO 1997-US20116	19971104
WO 9819649	A3	19980625		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9851973	A1	19980529	AU 1998-51973	19971104
EP 963200	A2	19991215	EP 1997-946884	19971104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1996-28708P P 19961105
US 1997-963058 A 19971103
WO 1997-US20116 W 19971104
OTHER SOURCE(S): MARPAT 129:12742
AB A group of compds. that effectively inhibit angiogenesis is provided. More specifically, **thalidomide** and various related compds.,e.g. **thalidomide** precursors, analogs, metabolites and hydrolysis products, have been shown to inhibit angiogenesis and to treat disease states resulting from angiogenesis. Addnl., antiinflammatory drugs, such as steroids and **NSAIDs** can inhibit angiogenesis-dependent diseases either alone or in combination with **thalidomide** and related compds. Importantly, these compds. can be administered orally.

L144 ANSWER 16 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:816444 HCAPLUS
DOCUMENT NUMBER: 135:352829
TITLE: Combination therapeutic compositions containing benzene compounds
INVENTOR(S): Jaen, Juan C.; Chen, Jin-Long
PATENT ASSIGNEE(S): Tularik Inc., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001082916	A2	20011108	WO 2001-US14393	20010502
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,				

LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-201613P P 20000503
OTHER SOURCE(S): MARPAT 135:352829
AB The present invention provides pharmaceutical compns. and methods for the treatment of diabetes mellitus using combination therapy. The compns. relate to a benzene compd. and an antidiabetic agent such as sulfonylureas, biguanides, glitazones, .alpha.-glucosidase inhibitors, potassium channel antagonists, aldose reductase inhibitors, glucagon antagonists, activators of RXR, insulin therapy or other anti-obesity agent. The methods include the administration of the combination of benzene compd. with antidiabetic agent where the two components are delivered in a simultaneous manner, where the benzene compd. is administered first, followed by the antidiabetic agent, as well as wherein the antidiabetic agent is delivered first followed by the benzene compd. For example, the benzene compd. (I) was synthesized using a 5-amino-2-(3-chloro-5-pyridyloxy)benzonitrile (0.457 g) in methylene chloride to which was added 2,4-dichlorobenzenesulfonyl chloride (0.456 g), followed by pyridine (150 .mu.L). The reaction progress was monitored by TLC, and upon completion the solvent was removed under vacuum. The resulting residue was partitioned between methylene chloride and water. The org. layer was drawn off and concd. The residue was triturated with ether to provide 0.447 g of I as a white solid, m.p. 154-156.degree..

L144 ANSWER 17 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:677067 HCAPLUS
DOCUMENT NUMBER: 135:251931
TITLE: Function homology screening method, and use in identification of drug candidates
INVENTOR(S): Berg, Ellen L.; Butcher, Eugene C.; Melrose, Jennifer; Plavec, Ivan
PATENT ASSIGNEE(S): Bioseek, Inc., USA
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001067103	A1	20010913	WO 2001-US7190	20010306

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-186976P P 20000306
US 2000-195672P P 20000407
AB A method is provided for screening biol. active agents based on the anal. of complex biol. responses in culture. Methods for selecting cells and culture conditions for such screens are provided, as well as the identification of an optimized set of discrete parameters to be measured, and the use of biomap anal. for rapid identification and characterization of drug candidates, genetic sequences acting pathways, and the like. A

feature of the invention is simultaneous screening of a large no. of cellular pathways, and the rapid identification of compds. that cause cellular responses.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L144 ANSWER 18 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:456950 HCAPLUS
DOCUMENT NUMBER: 133:84244
TITLE: Method of using a cyclooxygenase-2 inhibitor and an integrin antagonist as a combination therapy in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle & Co., USA
SOURCE: PCT Int. Appl., 348 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038786	A2	20000706	WO 1999-US30692	19991222
WO 2000038786	A3	20010308		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1140179	A2	20011010	EP 1999-966594	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
WO 1999-US30692 W 19991222

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a cyclooxygenase-2 inhibitor, an integrin antagonist and an antineoplastic agent.

L144 ANSWER 19 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:456927 HCAPLUS
DOCUMENT NUMBER: 133:84243
TITLE: Method of using a cyclooxygenase-2 inhibitor and one or more antineoplastic agents as a combination therapy in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 236 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000038730	A2	20000706	WO 1999-US30693	19991222
WO 2000038730	A3	20001102		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1140192	A2	20011010	EP 1999-967543	19991222

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

NO 2001003155	A	20010822	NO 2001-3155	20010622

PRIORITY APPLN. INFO.:	US 1998-113786P	P	19981223
	WO 1999-US30693	W	19991222

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a cyclooxygenase-2 inhibitor and an antineoplastic agent.

L144 ANSWER 20 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:456866 HCAPLUS
DOCUMENT NUMBER: 133:84239
TITLE: Method of using an integrin antagonist and one or more antineoplastic agents as a combination therapy in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G. D. Searle & Co., USA
SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038665	A2	20000706	WO 1999-US30670	19991222
WO 2000038665	A3	20001116		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1140193	A2	20011010	EP 1999-968529	19991222

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:	US 1998-113786P	P	19981223
	WO 1999-US30670	W	19991222

AB The present invention provides methods to treat or prevent neoplasia disorders in a mammal using a combination of an integrin antagonist and an antineoplastic agent.

L144 ANSWER 21 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:441655 HCAPLUS

DOCUMENT NUMBER: 133:68922
TITLE: Method of using a cyclooxygenase-2 inhibitor and a matrix metalloproteinase inhibitor as a combination therapy in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle & Co., USA
SOURCE: PCT Int. Appl., 437 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037107	A2	20000629	WO 1999-US30776	19991222
WO 2000037107	A3	20010201		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1140194	A2	20011010	EP 1999-968540	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001003156	A	20010823	NO 2001-3156	20010622

PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
WO 1999-US30776 W 19991222

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a cyclooxygenase-2 inhibitor, a matrix metalloproteinase inhibitor and an antineoplastic agent.

L144 ANSWER 22 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:672623 HCAPLUS
DOCUMENT NUMBER: 131:295603
TITLE: Enhancement of antibody-cytokine fusion protein-mediated immune responses by co-administration with an angiogenesis inhibitor
INVENTOR(S): Gillies, Stephen D.
PATENT ASSIGNEE(S): Lexigen Pharmaceuticals Corp., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952562	A2	19991021	WO 1999-US8335	19990415
WO 9952562	A3	19991118		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9935650	A1	19991101	AU 1999-35650	19990415
EP 1071468	A2	20010131	EP 1999-917558	19990415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9909583	A	20020115	BR 1999-9583	19990415
NO 2000005155	A	20001213	NO 2000-5155	20001013
PRIORITY APPLN. INFO.:			US 1998-81863P P	19980415
			WO 1999-US8335 W	19990415

AB Compns. and methods are disclosed for enhancing a cytocidal immune response directed against a preselected cell-type in a mammal. The methods and compns. rely on a combination of an antibody-cytokine immunoconjugate and an angiogenesis inhibitor. Once administered to the mammal, the immunoconjugate induces an immune response against the preselected cell-type, for example, a cancer cell which, as a result of the synergy with the angiogenesis inhibitor, is greater than the immune response induced by the immunoconjugate alone. The methods and compns. are particularly useful at killing solid tumors or virally-infected cells in a mammal.

L144 ANSWER 23 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002053357 EMBASE
TITLE: Could less be more? Low-dose chemotherapy goes on trial.
AUTHOR: Garber K.
SOURCE: Journal of the National Cancer Institute, (16 Jan 2002) 94/2 (82-84).
ISSN: 0027-8874 CODEN: JNCIAM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
037 Drug Literature Index
LANGUAGE: English

L144 ANSWER 24 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001086621 EMBASE
TITLE: Pharmacokinetics, safety, and tolerability of BAY 12-9566 and nonsteroidal anti-inflammatory agents (naproxen, ibuprofen) during coadministration in patients with osteoarthritis.
AUTHOR: Shah A.; Woodruff M.; Agarwal V.; Liu P.; Sundaresan P.
CORPORATE SOURCE: Dr. A. Shah, Bayer Corporation, 400 Morgan Lane, West Haven, CT 06516-4175, United States
SOURCE: Journal of Clinical Pharmacology, (2001) 41/3 (330-339).
Refs: 24
ISSN: 0091-2700 CODEN: JCPCBR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The pharmacokinetic interactions between BAY 12-9566 and two nonsteroidal anti-inflammatory drugs (NSAIDs), naproxen and ibuprofen, were investigated in osteoarthritis (OA) patients. The study comprised six groups: two NSAID groups with three levels of treatment (BAY 12-9566 400 mg, BAY 12-9566 100 mg, and placebo). Plasma pharmacokinetic parameters (AUC(0-.tau.), C(max), and t(max)) were determined for each treatment group following 5 days of NSAID administration, 14 days of BAY 12-9566

administration, and 14 days of concurrent NSAID and BAY 12-9566 administration. For most conditions, the total plasma drug concentrations of both NSAID and BAY 12-9566 were diminished by coadministration; total plasma BAY 12-9566 was not affected by ibuprofen treatment. Importantly, the free drug concentrations were largely unaffected by coadministration. Most side effects were mild or moderate in intensity, and all events, with the exception of headache, were reported in both NSAID groups and in both placebo and BAY 12-9566 groups. .COPYRGT. 2001 the American College of Clinical Pharmacology.

L144 ANSWER 25 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001380552 EMBASE
TITLE: Drugs targeted against protein kinases.
AUTHOR: Kumar C.C.; Madison V.
CORPORATE SOURCE: C.C. Kumar, Department of Tumour Biology, Schering-Plough Research Institute, 2015 Galloping Hill Road, Kenilworth, NJ 07033, United States. chandra.kumar@spcorp.com
SOURCE: Emerging Drugs, (2001) 6/2 (303-315).
Refs: 41
ISSN: 1361-9195 CODEN: EMDRFV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Current treatments for cancer (surgery, radiation and chemotherapy) are successful for early stage localised disease but have severe side effects. New treatments are needed to increase the cure rate and life expectancy of patients. With the discovery of oncogenes, tumour suppressor genes and an understanding of their role in the development of the malignant disease, a new era of therapy has begun. Cancer is a manifestation of deregulated signalling pathways that mediate cell growth and programmed cell death. Protein kinases are essential elements in these signalling pathways. In the US, Novartis launched Gleevec.RTM. (imantinib, STI-571) in May 2001 as the first anti-cancer drug whose mechanism of action is kinase inhibition. In Phase 1 trials, 23/24 patients with chronic myelogenous leukaemia (CML) had complete remissions and the drug is relatively non-toxic. Herceptin.RTM. (trastuzumab) is a monoclonal antibody (mAb) against a member of the growth factor receptor family (HER-2/neu) that was launched in 1998 by Genentech for the treatment of breast cancer. Trastuzumab has an excellent antitumour profile, particularly when used in combination with doxorubicin and paclitaxol. These drugs are pioneering the treatment of cancer based on the molecular understanding of the disease. Numerous drugs that target growth factor receptors and their signalling pathways are in advanced clinical trials. Herein, antibodies against receptors and small molecule inhibitors of kinases in signalling pathways will be summarised. Inter-disciplinary preclinical studies have identified chemicals that target specific kinases. We believe that clinical studies of these agents will yield new anticancer agents that target specific diseases and that are less toxic than current agents.

L144 ANSWER 26 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001304397 EMBASE
TITLE: Recent advances in the chemotherapy of non-small cell lung cancer.
AUTHOR: Inoue A.; Saijo N.
CORPORATE SOURCE: N. Saijo, Medical Oncology Division, National Cancer Center Hospital, 1-1 Tsukiji 5-chome, Chuo-ku, Tokyo 104-0045, Japan
SOURCE: Japanese Journal of Clinical Oncology, (2001) 31/7

(299-304).
Refs: 51
ISSN: 0368-2811 CODEN: JJCOAC
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
038 Adverse Reactions Titles
037 Drug Literature Index
036 Health Policy, Economics and Management
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Chemotherapeutic regimens containing new anticancer agents in combination with cisplatin and carboplatin have been demonstrated to be equivalently active against advanced non-small cell lung cancer. The choice of a chemotherapeutic regimen depends on differences in time to progression, response rate, toxicity profile, cost and symptom relief. Several other strategies, such as three-drug combinations, sequential use of a third drug, weekly administration, et., have been evaluated to improve the chemotherapeutic effect. The sequencing of the human genome may permit targeting of specific abnormalities related to each lung cancer with target-based drugs. This should increase the possibility of application of individualized therapy and, we would hope, improve survival.

L144 ANSWER 27 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000217121 EMBASE
TITLE: Angiogenesis and surgery: From mice to man.
AUTHOR: Drixler T.A.; Voest E.E.; Van Vroonhoven T.J.M.V.; Borel Rinkes I.H.M.
CORPORATE SOURCE: Dr. I.H.M. Borel Rinkes, Department of Surgery, University Medical Center, P.O. Box 85500, NL-3508 GA Utrecht, Netherlands
SOURCE: European Journal of Surgery, (2000) 166/6 (435-446).
Refs: 116
ISSN: 1102-4151 CODEN: EUJSEH
COUNTRY: Norway
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
009 Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L144 ANSWER 28 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000132226 EMBASE
TITLE: Inhibition of diclofenac formulated in hyaluronan on angiogenesis in vitro and its intraocular tolerance in the rabbit eye.
AUTHOR: Shen W.-Y.; Constable I.J.; Chelva E.; Rakoczy P.E.
CORPORATE SOURCE: W.-Y. Shen, Department Molecular Ophthalmology, Lions Eye Institute, 2 Verdun Street, Nedlands, Perth, WA 6009, Australia. shen@cyllene.uwa.edu.au
SOURCE: Graefe's Archive for Clinical and Experimental Ophthalmology, (2000) 238/3 (273-282).
Refs: 37
ISSN: 0721-832X CODEN: GACODL
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English

SUMMARY LANGUAGE: English

AB Purpose: To investigate the effect of diclofenac, a potent nonsteroidal anti-inflammatory drug, formulated in hyaluronan (diclofenac/HA) on angiogenesis in vitro and its intraocular toxicity in vivo. Methods: The effect of diclofenac/HA on angiogenesis was determined by choriocapillary endothelial cells on Matrigel stimulated by vascular endothelial growth factor (VEGF). The tube areas were quantified by image digital analysis. For toxicity study, diclofenac/HA was injected intravitreally with a dose range from 100 to 1080 .mu.g in 26 rabbits following gas compression vitrectomy. Potential toxicity was assessed by indirect ophthalmoscopy and by histological studies (light and electron microscopy). Retinal function was monitored by electroretinography (ERG) in six rabbits that received 400 .mu.g of diclofenac/HA. Results: Diclofenac/HA, 180, 90 .mu.g/ml, inhibited tube formation to 24% and 55% of the standard group (Media Ham's F12 plus 5% fetal calf serum and 50 ng/ml VEGF) respectively ($P < 0.01$). Intravitreal injection of 540 .mu.g or higher doses of diclofenac/HA resulted in ocular toxicity in the rabbit, demonstrated as cataract, vitreous haze and retinal damage observed by indirect ophthalmoscopy and light- and electronmicroscopic examinations. No toxicity was observed in the eyes that received 400 .mu.g or less diclofenac/HA, which was further supported by the normal ERG examined at 4 and 25 days post injection. Conclusions: Diclofenac/HA inhibits tube formation in vitro and is nontoxic to the rabbit retina at concentrations that are inhibitory to tube formation. Our results suggest diclofenac/HA may be an effective candidate to inhibit ocular neovascularisation related to granulomatous reaction in the eye.

L144 ANSWER 29 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999404666 EMBASE
TITLE: The effect of selective cyclooxygenase-2 inhibitor on corneal angiogenesis in the rat.
AUTHOR: Yamada M.; Kawai M.; Kawai Y.; Mashima Y.
CORPORATE SOURCE: Dr. M. Yamada, Department of Ophthalmology, Keio University, School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160, Japan. yamadam@med.keio.ac.jp
SOURCE: Current Eye Research, (1999) 19/4 (300-304).
Refs: 23
ISSN: 0271-3683 CODEN: CEYRDM
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Purpose. Eicosanoids that are present in inflamed tissues are thought to play a significant role in angiogenesis. Cyclooxygenase, a key enzyme in eicosanoid synthesis, has recently been shown to exist in two isoforms: the constitutive COX-1 and the inducible COX-2. This study was undertaken to determine the role of COX-2 in the corneal angiogenic response. Methods. Angiogenesis in the rat cornea was provoked by chemical cautery. Either NS-398, a selective COX-2 inhibitor, or indomethacin, a non-selective COX inhibitor, was applied topically 3 times daily for 4 days. Neovascularization was quantitated by digital image analysis in corneal flat preparations. To test their inhibitory effects on eicosanoid synthesis, normal or cauterized corneas were incubated in the culture medium with the inhibitor. Prostaglandin E2 in the medium was assayed using an enzyme-linked immunosorbent assay. Results. Both NS-398 and indomethacin significantly inhibited corneal neovascularization with the % inhibition of 36.4 .+-. 9.6%, and 38.5 .+-. 9.0%, respectively, when applied topically at a concentration of 0.1% ($p < .001$). Neither reduced the angiogenic response at a concentration of 0.01% or below. PGE2 production in the cauterized cornea was 2.0 times higher than that in the controls. In normal corneas, indomethacin inhibited PGE2 synthesis by 80%,

whereas NS-398 inhibited it by no more than 20%. In contrast, in injured corneas, both indomethacin and NS-398 inhibited PGE2 synthesis in a similar fashion, with a maximal inhibition rate of 75 to 80%. Conclusions. Our results suggest that COX-2 induction in cauterized corneas increases the level of eicosanoids, which result in corneal angiogenesis.

L144 ANSWER 30 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999302714 EMBASE
TITLE: Future developments of antipsoriatic therapy.
AUTHOR: Beissert S.; Luger T.A.
CORPORATE SOURCE: Dr. S. Beissert, Department of Dermatology, University of Munster, Munster, Germany
SOURCE: Dermatologic Therapy, (1999) 11/- (104-117).
Refs: 131
ISSN: 1396-0296 CODEN: DETHFE
COUNTRY: Denmark
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 013 Dermatology and Venereology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L144 ANSWER 31 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999004247 EMBASE
TITLE: Inhibition of angiogenesis by sulindac and its sulfone metabolite (FGN- 1): A potential mechanism for their antineoplastic properties.
AUTHOR: Skopinska-Rozewska E.; Piazza G.A.; Sommer E.; Pamukcu R.; Barcz E.; Filewska M.; Kupis W.; Caban R.; Rudzinski P.; Bogdan J.; Mlekodaj S.; Sikorska E.
CORPORATE SOURCE: E. Skopinska-Rozewska, Department of Immunology, National Institute of TB/Lung Dis., 26 Plocka Street, 01138 Warsaw, Poland
SOURCE: International Journal of Tissue Reactions, (1998) 20/3 (85-89).
Refs: 16
ISSN: 0250-0868 CODEN: IJTEDP
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 013 Dermatology and Venereology
016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The nonsteroidal antiinflammatory drug sulindac (sulfoxide) is known to cause regression and prevent recurrence of adenomas in patients with familial adenomatous polyposis. The mechanism of action does not appear to require inhibition of prostaglandin synthesis since the sulfone metabolite of sulindac (FGN-1) retains the antineoplastic properties of sulindac but lacks inhibitory effects on cyclooxygenase, types 1 and 2. FGN-1 has been shown to induce apoptosis in a variety of tumor cell lines, and selective apoptosis of neoplastic cells has been proposed to account for its antineoplastic properties. Since angiogenesis is necessary for tumor progression and may be related to apoptosis, it is possible that inhibition of angiogenesis may also contribute to the antineoplastic properties of sulindac or FGN-1. In order to test this possibility, cells derived from several different types of human lung tumors were grafted intradermally in Balb/c mice. Sulindac sulfoxide and its sulfide and sulfone metabolites were administered for 3 days orally, in a daily dose of 0.025-0.5 mg, and angiogenesis was measured after 72 h using a previously described method. The results showed that sulindac sulfoxide and sulfone statistically inhibited angiogenesis.

L144 ANSWER 32 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96089904 EMBASE
DOCUMENT NUMBER: 1996089904
TITLE: Treatment of **Kaposi**'s sarcoma.
AUTHOR: Tur E.; Brenner S.
SOURCE: Archives of Dermatology, (1996) 132/3 (327-331).
ISSN: 0003-987X CODEN: ARDEAC
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
013 Dermatology and Venereology
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The classic form of **Kaposi**'s sarcoma (KS) is a rare multifocal neoplasm, as described by **Kaposi** in 1872. One hundred nine years after **Kaposi**'s first description of the disease, the interest in all aspects of this disease escalated because of the emergence of human immunodeficiency virus (HIV), which is frequently accompanied by KS. This prompted zealous research, as reflected by numerous reports. Despite recent important discoveries, we are still far from understanding the pathogenesis of the disease and the mechanism of action of its various treatment modalities. As of today, treatment consists of most of the old modalities, some old ones in an updated improved version, and some new and experimental therapies. Our purpose is to focus on recent or novel data and to mention available treatments and their advantages, disadvantages, and side effects. We will also speculate on future directions.

L144 ANSWER 33 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96085520 EMBASE
DOCUMENT NUMBER: 1996085520
TITLE: Combination therapy in rheumatoid arthritis: The animal model perspective.
AUTHOR: Oliver S.J.; Brahn E.
CORPORATE SOURCE: Division of Rheumatology, UCLA, School of Medicine, 1000 Veteran Avenue,Los Angeles, CA 90095, United States
SOURCE: Journal of Rheumatology, (1996) 23/SUPPL. 44 (56-60).
ISSN: 0315-162X CODEN: JRHUA
COUNTRY: Canada
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Attempts to improve antirheumatic agent efficacy have resulted in exploration of treatment protocols with combinations of 2 or more agents. Hypothetically, an ideal combination therapy would have greater efficacy and less toxicity than any of its component agents used individually. However, even a limited number of available drugs can produce a daunting number of possible combination protocols, each requiring clinical evaluation. Intelligent selection of combination protocols, based on a firm understanding of each agent's specific mechanism(s) of action, may help identify potentially useful regimens. Autoimmune animal models of inflammatory synovitis provide a unique opportunity to study the etiology, pathophysiology, and treatment of rheumatoid arthritis (RA). Induction-of chronic inflammatory synovitis in susceptible inbred strains can allow for in vivo study under repro ducible controlled conditions, using experimental protocols not possible in humans. Although animal models can only approximate human rheumatic disease in its complete form, they are

nonetheless important for developing new therapeutic strategies. We review the 3 most common animal models of RA, the streptococcal cell wall, adjuvant, and collagen arthritis rat models. Surprisingly, few published studies evaluate combination therapy in RA animal models. We discuss these investigations, which use interventions aimed at angiogenesis, microtubule function, and immune regulation as examples of animal models to. assess and develop effective therapeutic combinations of antirheumatic agents.

L144 ANSWER 34 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95070095 EMBASE
DOCUMENT NUMBER: 1995070095
TITLE: Effect of intravitreal administration of indomethacin on experimental subretinal neovascularization in the subhuman primate.
AUTHOR: Sakamoto T.; Soriano D.; Nassaralla J.; Murphy T.L.; Oganesian A.; Spee C.; Hinton D.R.; Ryan S.J.
CORPORATE SOURCE: Doheny Eye Institute, 1450 San Pablo St,Los Angeles, CA 90033, United States
SOURCE: Archives of Ophthalmology, (1995) 113/2 (222-226). ISSN: 0003-9950 CODEN: AROPAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objectives: To examine the effect of indomethacin, a cyclooxygenase (CO) inhibitor, on laser-induced subretinal neovascularization (SRN) in the monkey. The CO pathway of arachidonic acid metabolism plays an important role in angiogenesis, and the inhibition of CO is known to inhibit angiogenesis in the cornea and in certain tumors. Materials and Methods: A cannula was implanted into the vitreous cavity of 11 eyes of six monkeys and connected to an osmotic minipump. Indomethacin (25 .mu.g/d) was delivered into the vitreous through the cannula for 14 days (seven eyes). Vehicle alone was injected for 14 days as a control (four eyes). Argon laser photocoagulation was then performed (eight spots at the posterior pole in each eye) to induce SRN. Fundus photographs and fluorescein angiograms were taken periodically to document the evolution of SRN. Light and electron microscopic examination was performed on two eyes of each group 8 weeks after photocoagulation. Results: Subretinal neovascularization developed from 2 to 4 weeks after photocoagulation. The incidence of SRN, indicated by fluorescein leakage, was significantly lower (P<.05) in the group treated with indomethacin (14.3%, eight of 56 lesions) than in the control group (37.5%, 12 of 32 lesions). After 8 weeks, no fluorescein leakage was found in either the control or indomethacin-treated groups. Scar formation was found on histologic examination in both groups. No histologic evidence of indomethacin toxicity was seen in the adjacent retina. Conclusions: Intravitreal administration of indomethacin inhibits the formation of laser-induced SRN in monkey eyes. This is consistent with the participation of the CO pathway in the process of SRN formation and suggests that this pathway could be a potential target in the treatment of SRN.

L144 ANSWER 35 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97329168 EMBASE
DOCUMENT NUMBER: 1997329168
TITLE: Subretinal neovascularization and possible hyaluronan-targeted therapy.
AUTHOR: Constable I.; Falk R.E.; Klein E.S.; Seed M.P.; Russell A.; Turley E.
CORPORATE SOURCE: I. Constable, Hyal Pharmaceutical Australia Ltd, Lions Eye Institute, 2 Verdun Street, Nedlands, WA 6009, Australia
SOURCE: Round Table Series - Royal Society of Medicine, (1995) -/40

(140-142).
Refs: 0
ISSN: 0268-3091 CODEN: RTSSES
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
LANGUAGE: English

L144 ANSWER 36 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95178330 EMBASE
DOCUMENT NUMBER: 1995178330
TITLE: Angiogenesis and cancer metastases: Therapeutic approaches.
AUTHOR: Teicher B.A.
CORPORATE SOURCE: Dana-Farber Cancer Institute, 44 Binney Street,Boston, MA 02115, United States
SOURCE: Critical Reviews in Oncology/Hematology, (1995) 20/1-2 (9-39).
ISSN: 1040-8428 CODEN: CCRHEC
COUNTRY: Ireland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
LANGUAGE: English

L144 ANSWER 37 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92039173 EMBASE
DOCUMENT NUMBER: 1992039173
TITLE: Angiogenesis and its inhibition: Potential new therapies in oncology and non-neoplastic diseases.
AUTHOR: Billington D.C.
CORPORATE SOURCE: Institut de Recherches Servier, 11 Rue des Moulineaux, 92150 Suresnes, France
SOURCE: Drug Design and Discovery, (1991) 8/1 (3-35).
ISSN: 1055-9612 CODEN: DDDIEV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The ability to mount an angiogenic response is probably present in all tissues, and stimulation of endothelial cells by any one of a wide variety of factors initiates a cascade of events leading to angiogenesis. In most tissues the overall lack of angiogenesis in normal situations probably results from the interaction of a complex series of multifactorial systems, each of which maintained in a state of balance between stimulation and inhibition. An imbalance in any one these systems, for example by an increase in the concentration of a growth factor, may lead to angiogenesis. Inhibition of angiogenic stimuli is unlikely to be effective as an approach to new angiostatic drugs, given the multiple stimulatory pathways available. Tumour cells for example may induce angiogenesis via release of nuemerous growth factors, prostaglandins ect, and by their attraction of inflammatory cells which in turn release multiple angiogenic stimuli. Inhibitory modulation of many of the individual steps of capillary growth which occur following an angiogenic stimulus can block the angiogenic response. This leads to the expectation that an effective inhibitor of a single key step in this cascade would be able to completely suppress angiogenesis. Inappropriate angiogenesis is an important factor in many disease including cancer and arthritis. In particular angiogenesis is an absolute requirement for neoplastic growth of solid tumours, and the establishment of secondary growths. There is

also a strong link between induction of angiogenesis by a tumour and its ability to metastasise.

L144 ANSWER 38 OF 43 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2002-075227 [10] WPIDS
DOC. NO. CPI: C2002-022418
TITLE: Use of interleukin-18 inhibitor for manufacture of medicament for treatment and/or prevention of atherosclerosis, thrombosis of atherosclerotic plaque, atherosclerotic plaque ulcer and heart failure recurrent events.
DERWENT CLASS: B04 D16
INVENTOR(S): CHVATCHKO, Y; MALLAT, Z; TEDGUI, A
PATENT ASSIGNEE(S): (ISTF) ARS APPLIED RES SYSTEMS HOLDING NV; (INRM) INSERM INST NAT SANTE & RECH MEDICALE
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001085201	A2	20011115	(200210)*	EN	54
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001067390	A	20011120	(200219)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001085201	A2	WO 2001-EP4843	20010430
AU 2001067390	A	AU 2001-67390	20010430

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001067390	A	Based on	WO 200185201

PRIORITY APPLN. INFO: EP 2000-109606 20000505

AB WO 200185201 A UPAB: 20020213
NOVELTY - Use of interleukin-18 inhibitor (I) for manufacture of medicament for treatment and/or prevention of atherosclerosis, thrombosis of atherosclerotic plaque (AP), AP ulcer, AP destabilization, ischemic syndromes due to plaque destabilization, AP disruption, heart failure recurrent events, or as diagnostic marker for bad clinical prognosis in heart failure or recurrent events after first event of heart failure, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) use of an expression vector (II) comprising the coding sequence for (I) for the manufacture of a medicament for the treatment and/or prevention of atherosclerosis;

(2) use of a vector (III) for inducing and/or enhancing the endogenous production of (I) in a cell in the manufacture of a medicament for the treatment and/or prevention of atherosclerosis;

(3) use of a cell (IV) that has been genetically modified to produce (I) in the manufacture of a medicament for the treatment and/or prevention of atherosclerosis;

(4) treatment and/or prevention of atherosclerosis comprising

administering to a host an effective inhibiting amount of (I) or (II); and

(5) use of IL-18 as a diagnostic marker of a bad clinical prognosis in heart failure and of recurrent events after a first event of heart failure.

ACTIVITY - Antiarteriosclerotic; cardiant; vasotropic; antiulcer. Cultured human umbilical vein endothelial cells (HUVECs) were exposed for 16 hours to oxidized lipoprotein (oxLDL) in the presence or absence of interleukin-18 (IL-18) inhibitors such as IL-18 binding protein (IL-18BP) or anti-IL-18 antibody. 83% of HUVECs died after exposure to oxLDL. The co-incubation with IL-18BP or anti-IL-18 antibody almost totally rescued the cells from death. No death was observed using IL-18BP. 89% of the cells survived using the anti-IL-18 antibody. The results showed the protective effect of the two different IL-18 inhibitors against cells death due to apoptosis within atherosclerotic plaque.

MECHANISM OF ACTION - Inhibitor of interleukin-18.

USE - (I) is useful for the manufacture of a medicament for treatment and/or prevention of atherosclerosis, by administering to a host, an effective inhibiting amount of (I). (I) is also useful for the manufacture of a medicament for treatment and/or prevention of thrombosis of AP, AP ulcer, AP destabilization, ischemic syndromes due to plaque destabilization, AP disruption or heart failure recurrent events, where the heart failure is ischemic or non-ischemic. (I) is also useful as a diagnostic marker for bad clinical prognosis in heart failure or recurrent events after first event of heart failure. (II) is useful for the manufacture of a medicament for treatment and/or prevention of atherosclerosis, by administering (II) to a host. (III) or (IV) is useful for the manufacture of a medicament for treatment and/or prevention of atherosclerosis (claimed).

Dwg.0/9

L144 ANSWER 39 OF 43 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-514501 [56] WPIDS
DOC. NO. CPI: C2001-153732
TITLE: Composition comprising a combination of an oxidizing and/or reducing agent, a protein-denaturing agent, and a hapten, useful for treating neoplasms, tumors, and cancers.
DERWENT CLASS: B05 D16
INVENTOR(S): YU, B
PATENT ASSIGNEE(S): (YUBB-I) YU B
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001052868	A1	20010726	(200156)*	EN	83

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2001030977 A 20010731 (200171)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001052868	A1	WO 2001-US1737	20010118
AU 2001030977	A	AU 2001-30977	20010118

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001030977 A	Based on	WO 200152868

PRIORITY APPLN. INFO: US 2000-177024P 20000119

AB WO 200152868 A UPAB: 20011001

NOVELTY - A composition (I) comprising a combination of an oxidizing or reducing agent, a protein-denaturing agent, and a hapten, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a kit comprising the combination (I);

(2) an article of manufacture comprising:

(a) packaging material;

(b) the combination above; and

(c) a label indicating that the article is for treating neoplasms; and

(3) a method for treating neoplasm in a mammal comprising in situ administration to the neoplasm of a mammal, a hapten and a coagulation agent or treatment that causes coagulation of the neoplasm (an autologous immune response is generated against the neoplasm).

ACTIVITY - Cytostatic.

31 advanced stage IV liver cancer patients were treated using the new combination. Prior to procedure, patients were given a mild sedative or painkiller. Patients were calmed thoroughly and were also monitored by modern medial imaging. With local anesthesia, percutaneous puncture was administered directly into the tumor using a spinal needle connected to a high-power syringe containing a combination of ethanol, H2O2, anticancer drug AraC (8 mg/ml) and hemotoxilin (5 mg/ml). Combination was injected directly into the tumor and distributed throughout the matrix of the whole tumor. Sonic imaging showed the stranger echo imaging which indicated the coagulation area.

Following coagulation lysis and tumor cell death monitored by sonic imaging, which showed liquefied echo, tumor started to shrink and disappear. Normal tissues grew replacing the tumor. The process was monitored by medical imaging systems. The amount of the ingredients of the combination injected into the tumor was determined by the diameter of tumors (cm) with 2 ml of the combination for each centimeter.

Procedure was repeated in 1-2 weeks. On average, each patient was treated with the injection for 3 times. No severe side effects for all the treated patients was observed, although some patients experienced tolerable pain the injection site while a few had light fever during the first week. All side effects disappeared in about 1 week. No serious complications happened in any cases.

MECHANISM OF ACTION - Gene therapy.

USE - The combination and the methods are useful for treating neoplasms, tumors, and cancers, including neoplasm or cancer of the e.g. adrenal gland, anus, auditory nerve, bile ducts, bladder, bone, brain, breast, bruccal, central nervous system, cervix, colon, ear, endometrium, esophagus, eye, eyelids, fallopian tube, gastrointestinal tract, head and neck, heart, kidney, larynx, liver, lung, or mandible.

The combination and methods may further be used in treating tumors of mesenchymal origin (e.g. connective tissue and derivatives, or endothelial and related tissues blood vessels), epithelial origin (stratified squamous carcinoma, or basal cells of skin or adenexa), and tumors derived from more than one neoplastic cell types derived from more than one germ layers.

The treatment may be used with radiation therapy, before surgery for the pre-treatment of neoplasm for easier removal of the neoplastic mass and reduces the neoplasm metastasis rate, or with gene therapy.

Dwg.0/4

L144 ANSWER 40 OF 43 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-594404 [56] WPIDS

DOC. NO. CPI: C2000-177565
TITLE: Inhibiting first-pass effects of orally administered materials by co-administering with first-pass inhibitors, provides reliable and safe first pass effect inhibition using citrus-based compositions.
DERWENT CLASS: B02 D13
INVENTOR(S): HARRIS, J W
PATENT ASSIGNEE(S): (BIOA-N) BIOAVAILABILITY SYSTEMS LLC
COUNTRY COUNT: 89
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000054768	A1	20000921	(200056)*	EN	193

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000039977 A 20001004 (200101)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000054768	A1	WO 2000-US2517	20000217
AU 2000039977	A	AU 2000-39977	20000217

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000039977	A	Based on	WO 200054768

PRIORITY APPLN. INFO: US 1999-251467 19990217

AB WO 200054768 A UPAB: 20001106
NOVELTY - Novel method of inhibiting the first-pass effect of orally administered materials that are subject to a first-pass effect comprises co-administering to the patient the material and a second compound selected from spiro-fused heterocycles (I) or (II).

DETAILED DESCRIPTION - Novel method of inhibiting the first-pass effect of orally administered materials that are subject to a first-pass effect comprises co-administering to the patient the material and a second compound selected from spiro-fused heterocycles of formula (I) or (II).

INDEPENDENT CLAIMS are also included for:

(1) improved methods of designing inhibitors of enzymes or polypeptides, by modification of (I) or (II); and

(2) method for preparing grapefruit juice-derived solids preparations, comprising:

(a) passing grapefruit juice through an initial filter with a filter size at least 200 micro m to produce an initial filtrate; and passing the initial filtrate through a filter with a filter size of 25 - 75 micro m, thereby trapping the grapefruit-derived solids on the filter; or

(b) centrifuging the grapefruit juice at 1000 G for 10 minutes to produce a supernatant and a pellet, optionally resuspending the pellet in water and re-centrifuging to produce a washed pellet of grapefruit-derived solids.

USE - The methods are used to inhibit the first-pass effect of orally administered materials that are subject to a first-pass effect (claimed) such as drugs consisting of charged, uncharged, hydrophilic, zwitterionic and/or hydrophobic species including analgesics, antibiotics, antirheumatics, anti-asthmatics, muscle relaxants, narcotic antagonists,

non-steroidal anti-inflammatory drugs, anesthetics, anti-inflammatories, neuromuscular blockers, sedatives, antimicrobials, anti-arthritics, anticancer agents, aminoglycosides, antifungals, antimalarials, antiparasitics, antituberculars, anti-arrhythmics, antivirals, carbapenems, cephalosporins, fluoroquinolones, macrolides, penicillins, sulfonamides, tetracyclines, cardiovascular agents, cholinergic agonists, angiotensin II antagonists, angiotensin-converting enzyme inhibitors, protease inhibitors, renin inhibitors, anti-adrenergic agents, antidysrhythmics, antihyperlipidiemics, antihypotensives, antihypertensives, antiplatelet agents, beta blockers, calcium channel blockers, diuretics, nitrates, pressors, steroids, thrombolytics, contrast media, dermatology agents, antibacterials, endocrine and metabolic agents, androgens/anabolic steroids, bisphosphonates, corticosteroids, chemotherapeutics, anti-diabetics, gout-related agents, minerals, nutritionals, thyroid agents, vitamins, antihistamines, antitussives, decongestants, gastroenterology agents, anti-diarrheals, anti-emetics, anti-**ulcer** agents, hematology agents, anticoagulants, immunosuppressants, neurological agents, anticonvulsants, antimigraine agents, parkinsonism agents, obstetric and gynecology agents, estrogens, gonadotropin-releasing hormone agonists, appetite suppressants, hormone replacement **combinations**, labor-induction agents, hormonal agents, progestins, tocolytics, oncology agents, ophthalmology agents, corticosteroids, **glaucoma** agents, psychiatric agents, Alzheimer's disease agents, antidepressants, tranquilizers, antispasmodics, contraceptives, antimaniacs, antipsychotics, anxiolytics/hypnotics, drug-dependence therapy agents, sympathomimetics, stimulants, anorexiants, receptor agonists, receptor antagonists, pulmonary agents, urology agents, bladder spasm agents, erectile dysfunction agents, opioids, nephrolithiasis agents, prostate **cancer** agents and vasoconstrictors e.g. saquinavir, indinavir, L-deprenyl, tacrolimus, Sandimmune (RTM: cyclosporin A), Neoral, (RTM: cyclosporin A), nelfinavir, VX-478/141 W94, felodipine, nifedipine or sumatriptan as well as ABT-378, acebutolol, acyclovir, aldesleukin, alfentanil, alteplace, amikacin, amphotericin B, amprenavir, anistreplase, atacurium, auranofin, azithromycin, azthreonam, benazepril, bisulfan, bleomycin, bretylium, bromocriptine, budesonide, buspirone, capreomycin, carbenicillin, carboplatin, carmustine, carvedilol, cefaclor, cefonicid, cefoperazone, ceforanide, cefotaxime, cefotetan, ceftazidime, ceftizoxime, ceftriaxone, cephalothin, cephapirin, chlorpromazine, cisplatin, clemastine, cyclosporin, cytarabine, desipramine, didanosine, dobutamine, doxepin, doxorubicin, edrophonium, erythromycin, esmolol, ethosuximide, felodipine, fentanyl, flumazenil, fluorouracil, foscarnet, fosinopril, ganciclovir, gentamicin, heparin, hydralazine, imipramine, indinavir, isradipine, kanamycin, ketamine, labetolol, L-deprenyl, lidocaine, lincomycin, lisinopril, lovastatin, nelfinavir, mercaptopurine, methicillin, methohexital, metocurine, metoprolol, mezlocillin, morphine, moxalactam, nabumetone, nadolol, nafcillin, nalbuphine, naloxone, naltrexone, netilmicin, nicardipine, nicotine, nimodipine, nitrendipine, nitroglycerin, norfloxacin, octreotide, oxacillin, **paclitaxel**, pancuronium, pentamidine, pentoxifylline, pipercuronium, piperacillin, pravastatin, propranolol, pyridostigmine, rifabutin, rimantandine, saquinavir, scopolamine, selegiline, sertraline, simvastatin, spironolactone, streptokinase, streptomycin, sufentanil, sumatriptan, tacrine, tacrolimus, tamoxifen, teniposide, terbutaline, terfenadine, thiopental, ticarcillin, tipranavir, tobramycin, triamcinolone acetonide, tubocurarine, vancomycin, vecuronium, venlafaxine and verapamil.

ADVANTAGE - The methods provide reliable and safe compositions that are citrus-based and contain no, or reduced, amounts of low molecular weight phototoxic furocoumarins. They provide consistent first pass-inhibiting activity. They use first-pass inhibitors (bioenhancers and inhibitors) in non-natural and non-commercially occurring forms.
Dwg.0/2

L144 ANSWER 41 OF 43 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-601836 [57] WPIDS
DOC. NO. CPI: C2000-180024
TITLE: **Treating** ocular disorders and causing posterior vitreous disconnection or dis-insertion, using urea (derivatives), **non-steroidal antiinflammatory** agent, antimetabolite and/or compound capable of dissolution of hyaloid membrane.
DERWENT CLASS: B05
INVENTOR(S): CASTILLEJOS, D
PATENT ASSIGNEE(S): (VITR-N) VITREO-RETINAL TECHNOLOGIES INC
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000051620	A1	20000908	(200057)*	EN	27
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2000037201	A	20000921	(200065)		
EP 1165095	A1	20020102	(200209)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000051620	A1	WO 2000-US5587	20000302
AU 2000037201	A	AU 2000-37201	20000302
EP 1165095	A1	EP 2000-916034	20000302
		WO 2000-US5587	20000302

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000037201	A	Based on	WO 200051620
EP 1165095	A1	Based on	WO 200051620

PRIORITY APPLN. INFO: US 1999-122503P 19990302
AB WO 200051620 A UPAB: 20001109
NOVELTY - Treatment of various eye disorders including the proliferation of eye fibroblasts and also accelerating the clearance of hemorrhagic blood from the vitreous humor, involves administering urea (derivatives), a non-steroidal anti-inflammatory agent, an antimetabolite, and/or compound capable of causing non-enzymatic dissolution of the hyaloid membrane.

DETAILED DESCRIPTION - Method for (i) treating the proliferation of fibroblasts within the eye; (ii) treating or **preventing neovascularization** of ocular tissues; (iii) accelerating the clearance of hemorrhagic blood from the vitreous humor; (iv) causing non-enzymatic dissolution of the hyaloid interface and/or; (v) causing posterior vitreous detachment of disinsertion, comprises delivering into the posterior segment of the eye an agent selected from urea, one of its derivatives, a non-steroidal anti-inflammatory agent, an antimetabolite, and/or a compound capable of causing non-enzymatic dissolution of the hyaloid membrane.

ACTIVITY - Ophthalmological.
No activity data given.
USE - The method is performed for one of the following purposes:
(a) inducing vitreous detachment and/or disinsertion of the vitreous body from the retina and epiretinal membranes (PVD);
(b) causing non-enzymatic liquefaction of the vitreous humor;
(c) causing diffusion or preventing the accumulation of localized concentrations near the retina of substances that are injurious or pathogenic to the retina (e.g. angiogenic factors);
(d) causing dissolution of coagulum within the vitreous humor (as may occur following intravitreal hemorrhage);
(e) causing a solvent action on fibroblasts;
(f) inhibiting fibroblasts;
(g) inhibiting or preventing fibrosis associated with the presence of vitreous heme;
(h) inhibiting the proliferation of fibroblasts in ocular tissues;
(i) treating diabetic **retinopathy**;
(j) treating intravitreal hemorrhage and accelerating the clearance of hemorrhagic blood from the vitreous humor;
(k) inducing PVD and/or liquefaction of the vitreous prior to the performance of a vitrectomy thereby limiting the likelihood of **retinal detachment**, **retinal** tearing, re-stimulation of retinal hemorrhage or other complications of the vitrectomy procedure;
(l) treating vitreous traction associated with macular holes;
(m) treating **macular degeneration**;
(n) treating retinitis;
(o) prophylaxis to **retinal detachment** in patients who are at risk of it (e.g. high myopes);
(p) treating preretinal and sub retinal membranes;
(q) treating cystoid macular edema;
(r) pre-operative preparation of the eye in the surgical treatment of eye trauma;
(s) pre-operative treatment prior to certain types of **glaucoma** surgery (e.g. those performed in the treatment of neovascular **glaucoma**);
(t) treating occlusion of the central retinal vein or artery;
(u) treating conditions associated with neovascularization e.g. neovascular iris and neovascular **glaucoma**;
(v) treating ocular ischemic syndrome;
(x) treating conditions associated with posterior eye inflammation such as VKH, **pars planitis**, and **toxoplasmosis**
; and
(y) improving the delivery and bioavailability to the retina and other tissues of intravitreally administered drugs (all claimed).
ADVANTAGE - Inducing PVD with agents that cause non-enzymatic dissolution of the hyaloid membrane or hyaloid interface, results in detachment or disinsertion of the vitreous body from the retina, thereby allowing vitrectomy, repair of retinal tears or other procedures to be performed with a reduced chance of causing retinal tearing or hemorrhage, avoiding the disadvantages of traditional vitrectomy procedures.
Dwg.0/0

L144 ANSWER 42 OF 43 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-446803 [38] WPIDS
DOC. NO. CPI: C1998-135483
TITLE: New matrix metalloproteinase inhibitors - useful in treatment or prophylaxis of tumoural diseases, rheumatoid and osteoarthritis and inflammatory, infectious and immunological diseases.
DERWENT CLASS: B05
INVENTOR(S): ABRATE, F; ALPEGIANI, M; BISSOLINO, P; CORIGLI, R; JABES, D; LOMBROSO, M; PALLADINO, M; PERRONE, E; ABRATE, M F

PATENT ASSIGNEE(S): (PHAA) PHARMACIA & UPJOHN SPA
COUNTRY COUNT: 33
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9833788	A1	19980806	(199838)*	EN	132
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU BR CA CN HU IL JP KR MX NO NZ PL UA US					
AU 9862942	A	19980825	(199903)		
EP 960108	A1	19991201	(200001)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI NL PT SE					
US 6194451	B1	20010227	(200114)		
JP 2001511139	W	20010807	(200150)		154

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9833788	A1	WO 1998-EP531	19980123
AU 9862942	A	AU 1998-62942	19980123
EP 960108	A1	EP 1998-906901	19980123
		WO 1998-EP531	19980123
US 6194451	B1	WO 1998-EP531	19980123
		US 1999-355315	19990730
JP 2001511139	W	JP 1998-532543	19980123
		WO 1998-EP531	19980123

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9862942	A	Based on	WO 9833788
EP 960108	A1	Based on	WO 9833788
US 6194451	B1	Based on	WO 9833788
JP 2001511139	W	Based on	WO 9833788

PRIORITY APPLN. INFO: GB 1997-2088 19970131

AB WO 9833788 A UPAB: 19980923
Matrix metalloproteinase inhibitors of formula (I), their solvates, hydrates and salts, are new: W = -NHOH or -OH; R1 = hydroxymethyl or a hydroxymethyl derivative which is an ether, ester, carbonate, etc.; R2 = OH or protected OH; or CR1R2 = an optionally substituted ring of formula (B1)-(B4); R3 = -AI-X-(CH2)n-A; A = 1-10C alkyl, 2-10C alkenyl, 3-7C cycloalkyl, aryl or heterocyclyl, each optionally substituted; n= 0-5; -X- = direct bond, -O-, -S-, -SO-, etc.; -AI- = 1-10C alkylene, 2-6C alkenylene or phenylene; R4 = a group (C) or (D), A or AI-X-A; R6 =H or the side chain of a natural or non-natural alpha -amino acid; R7 = amino or -NH-A-, -NH-CH2-A or -NH-CH2CH2-A; R8 = methyl, ethyl, phenyl, etc.; R9 = H or methyl, ethyl, phenyl,etc.; or NR8R9 = (D') where the nitrogen atom and the phenyl ring are optionally substituted; R5 = H or methyl; or NR4R5 = an optionally substituted azaheterocyclyl ring.

USE - (I) are useful in treatment or prophylaxis of diseases mediated in mammals by a matrix metalloproteinase. They are useful in treatment or prophylaxis of tumoural diseases in man, in particular for the control of local spread of established **tumours** and for the inhibition of the growth of established or occult metastases, either alone or in **combination** with cytotoxic or cytostatic drugs or with **inhibitors** of **angiogenesis**. (I) are useful in treatment or prophylaxis of **rheumatoid arthritis** and osteoarthritis in man, alone or in **combination** with **non -steroidal** or steroidal **antiinflammatory** drugs or with immunosuppressive drugs. They are also useful in treatment or prophylaxis

of inflammatory, infectious and immunological diseases promoted by local or systemic release of soluble TNF.

ADVANTAGE - None given.

Dwg.0/0

L144 ANSWER 43 OF 43 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1996-514903 [51] WPIDS
DOC. NO. CPI: C1996-161202
TITLE: Use of **Aspirin** or Satigrel as angiogenesis inhibitors - in **treatment** of **cancer**, inflammation and diabetic **retinopathy**.
DERWENT CLASS: **B05**
PATENT ASSIGNEE(S): (EISA) EISAI CO LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 08268886	A	19961015	(199651)*		6

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 08268886	A	JP 1995-74744	19950331

PRIORITY APPLN. INFO: JP 1995-74744 19950331

AB JP 08268886 A UPAB: 19961219

Use of Satigrel of formula (I) or **Aspirin** or their salts as angiogenesis inhibitors.

USE - The **angiogenesis** inhibitors are useful in the **prevention** and treatment of cancer of the stomach, lungs, liver, large bowel, colon, rectum, pancreas, prostate, bladder, kidney, ovaries, uterus, breast and skin, as well as in treating or preventing malignant melanoma, basal cell carcinoma, keloids, inflammation and diabetic **retinopathy**. Daily dosage comprises 0.01-2000 (pref. 1-1000) mg and admin. is oral or by intravenous injection, suppositories or percutaneous injection.

ADVANTAGE - The agent is safe.

Dwg.0/1

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